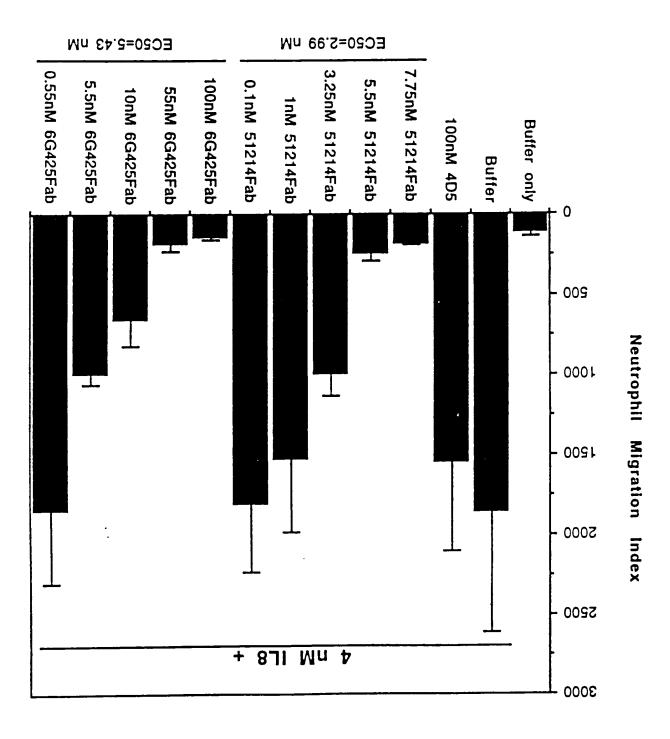
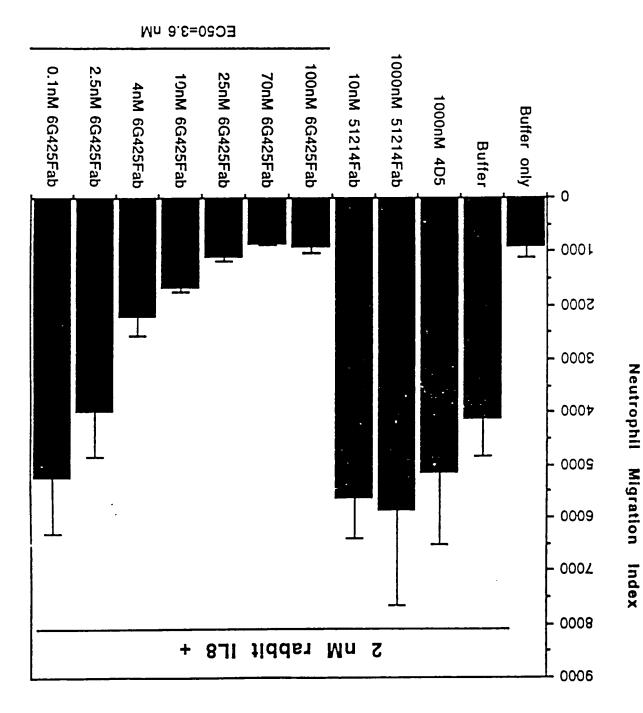
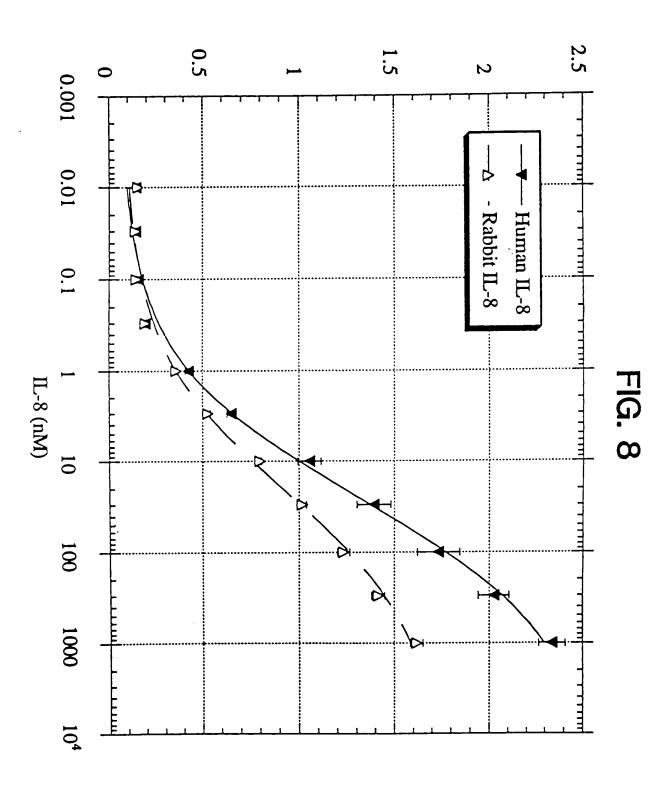
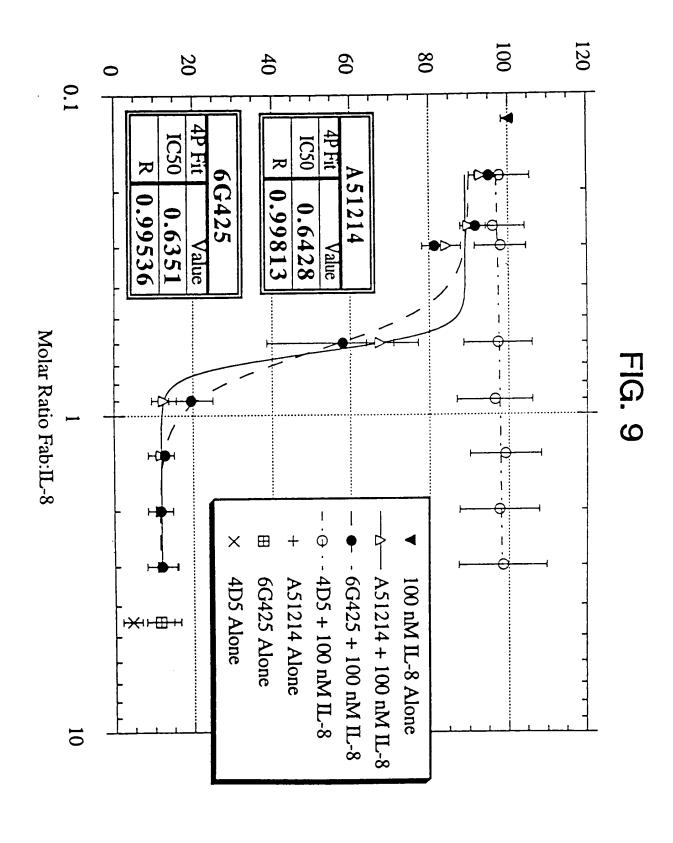


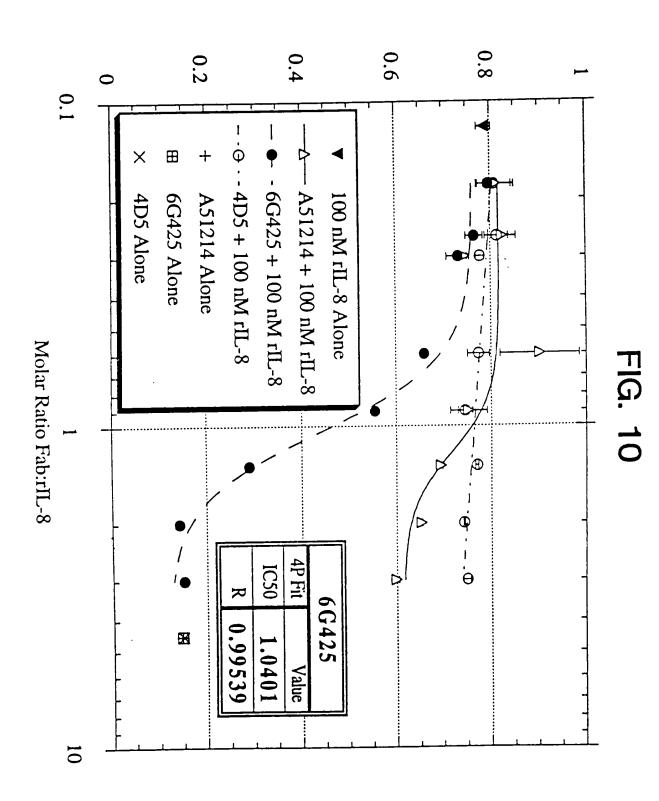
FIG. 6

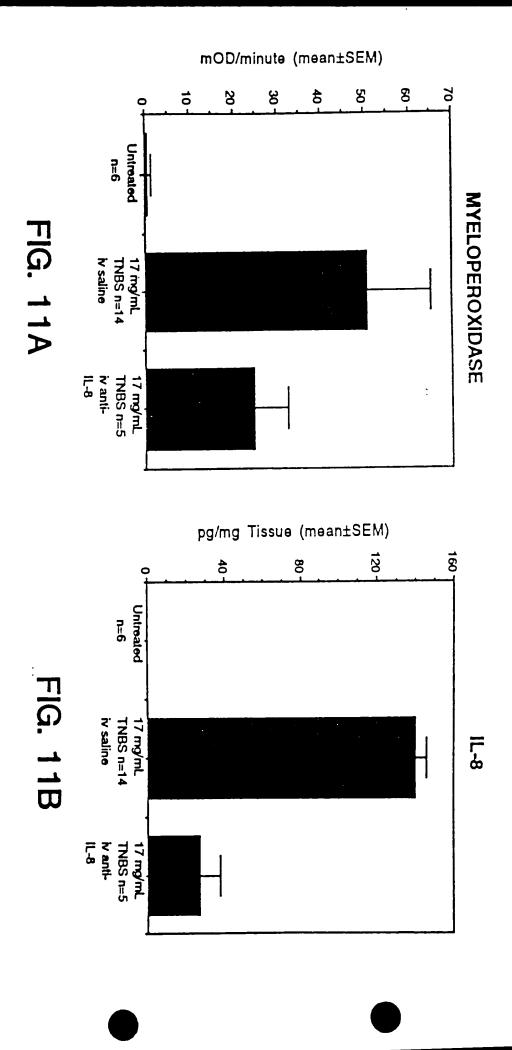


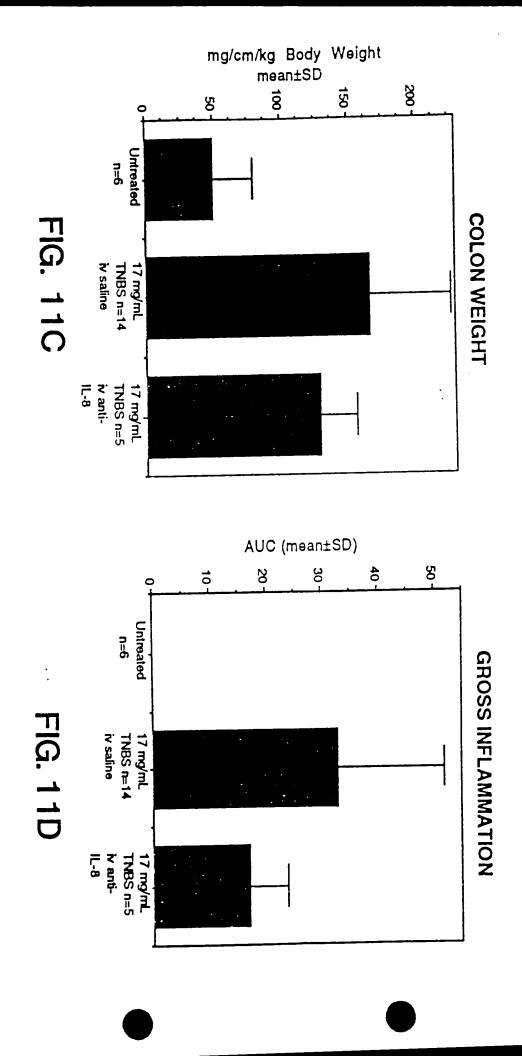


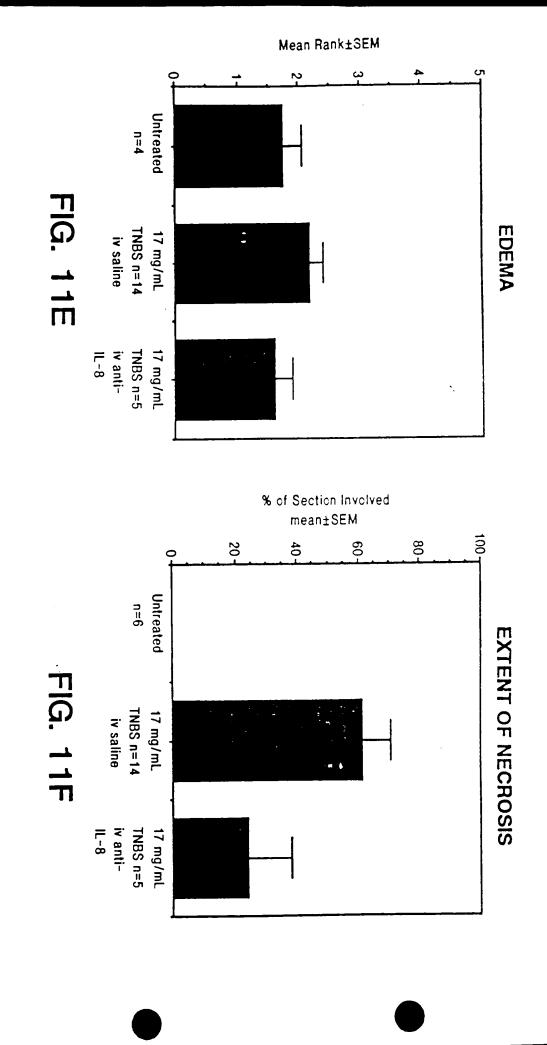


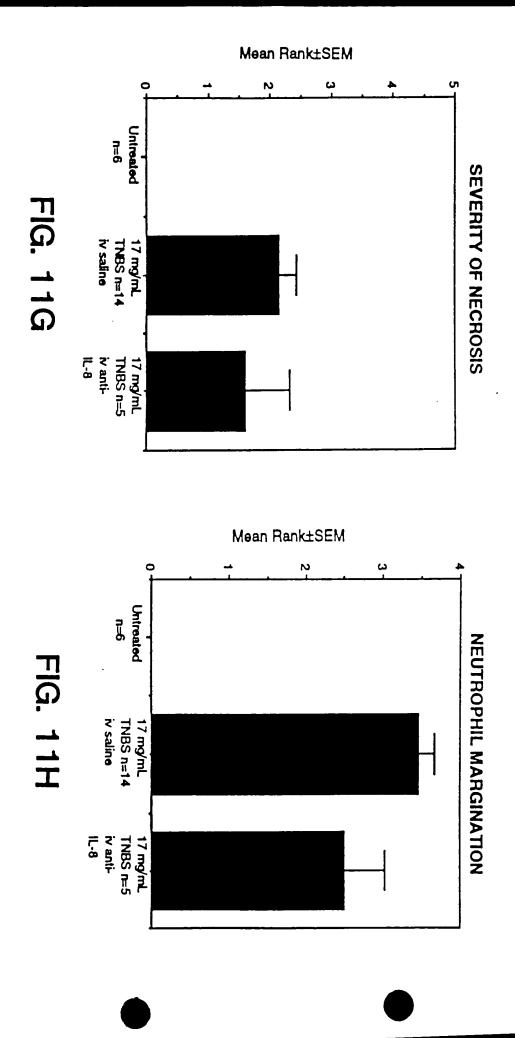


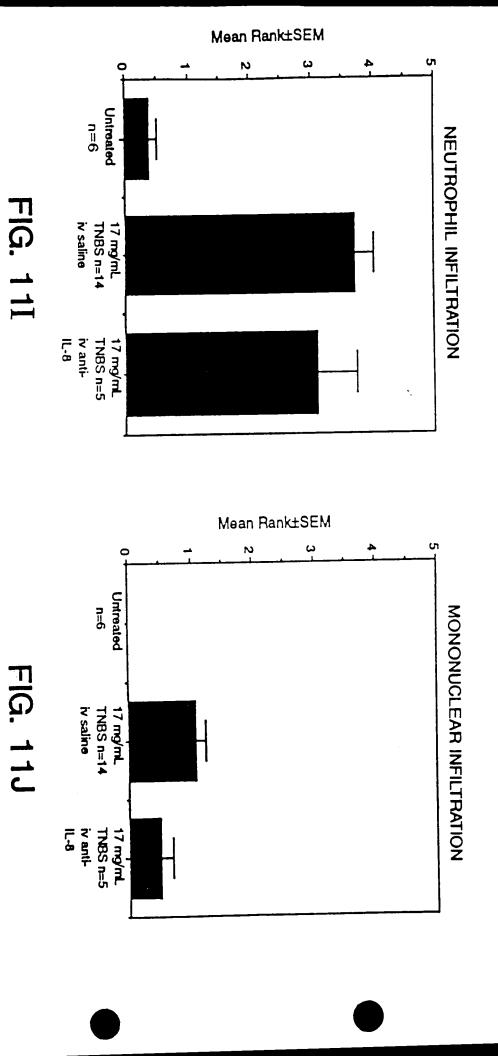


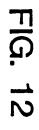


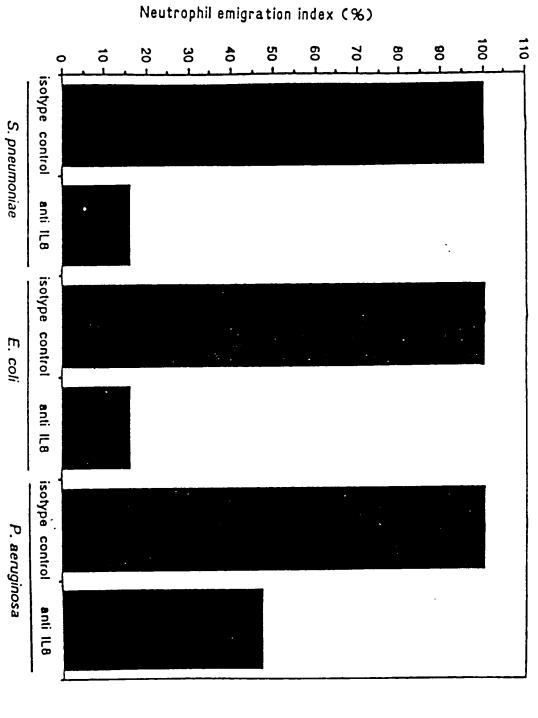












Group (n=5 rabbits per group)

Light Chain Primers:

MKTC-Z, ZZmer

MKTC-J' ZZWGz FIG. 13

'E DOĐOAĐĐAOTTĐTOAADOTĐAD 'Z

S GTGCTGCTGTGTATCTGTGC 3' (Z:011 OI 075)

(T :0N OI 0335)

WKTC-3' Szwer

SOUTO CAPTION OF THE PROPERTY (E:07 OI 773) IE

Heavy Chain Primers:

IGGSYC-I, 24mer

5 GCATCCTAGAGTCACCGAGGAGCC 3 (SEB ID NO: 4)

IGGSAC-2, 22mer

S:0v QE DECTCEGEGEAATAACCC 3' (SEW JD NO:5)

IGGSYC-3, SZmer

(9:0N (I 735) 

(b:00 05 435)

(3:00 7:193)

(人):河下海的

Light chain forward primer

SL001A-2 35 mer

A T  $\mathbf{T}$ 'E STEASSCATESTASTAS TSESATESSESAAASA 'S

Light chain reverse primer

SPOOTE 37 mer

5' GCTCTTCGAATG GTGGGAAGATGGATACAGTTGGTGC 3' (ARALL MIN)

Heavy chain forward primer FIG. 15

ZPOOSB 30 wer

'S SENTITETTETSESSEATGESSESSES 'S

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Heavy chain reverse primer

STOOSB 39-WER

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21:01 01 735)

(11:0701730)

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TGGAGTTGAA ACCTCAACTT E L K	CAGACTATTT GTCTGATAAA DYF	GCAGTGGATC CGTCACCTAG S G S	CTAAAGCACT GATTTCGTGA K A L	AGGCCAGTCA TCCGGTCAGT A S 0	TGACACAGTC ACTGTGTCAG T Q S
ACGGGCTGAT TGCCCGACTA R A D	CTGTCAGCAA GACAGTCGTT C Q Q C * *	TGGGACAGAT ACCCTGTCTA G T D	GATTTACTCG CTAAATGAGC I Y S	GAATGTGGGT CTTACACCCA N V G * * *	TCAAAAATTC AGTTTTTAAG Q K F
GCTGCACCAC CGACGTGGTG A A P P	TATAACATCT ATATTGTAGA Y N I Y * * * *	TTCACTCTCA AAGTGAGAGT F T L T	TCATCCTACC AGTAGGATGG S S Y R * * * * CDR #2	ACTAATGTAG TGATTACATC T N V A * * * *	ATGTCCACAT TACAGGTGTA M S T S
CAACTGTATC GTTGACATAG T V S	ATCCTCTCAC TAGGAGAGTG PLT * * *	CCATCAGCCA GGTAGTCGGT I S H	GGTACAGTGG CCATGTCACC Y S G * *	CCTGGTATCA GGACCATAGT W Y Q	CAGTAGGAGA GTCATCCTCT V G D
CATCTTCCCA GTAGAAGGGT I F P	GTTCGGTCCT CAAGCCAGGA F G P	TGTGCAGTCT ACACGTCAGA V Q S	AGTCCCTGAT TCAGGGACTA V P D	ACAGAAACCA TGTCTTTGGT Q K P	CAGGGTCAGC GTCCCAGTCG R V S

361 CCATTCGAA GGTAAGCTT 121 P F E

BstBI

(seb 30 NO: 16)

(5E6 SD NO:17)

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	TOTOT	DTADD	SSSA	DAADAA	AAD	) DDA:	DOTO	TOTE	)T)A	OTĐ	DTOT	SGAC	) DA	361
				E# 70	CI									
TGACCCGGT Q D W	* * <u>*</u> 5	W F	T *	4 <del>5</del>	S	¥ I	* 7 7999	* X 5	y Sem	ACA.	ÐΤΑΑ Υ	AAD/ F		٤6
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Ť:	CDB #													
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ATTDATDAOT TAAOTAOTDA V	TATAD ATATD	TTADD AATDD	TOTO ADAD	DDADDT DDTDDA	DTD DAD	OTO! ĐAĐ	TOAA ADTT	ADT:	) ) )	2555	ADDI	225	225	τ9
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		VH.rear 33-MER
(22:07 03 738)	، ٤	DOADTTDAADDOA <u>TDATOA</u> DD ' Z
		VH.front.SPE 21-MER
(17:34 (II DES)	. E	DDTTODAOOTODAAQOTTOTODAOTAODAOO ' 2
		VL.rear 31-MER
(25:27 (5 335)	، ٤	DADADTADTATADTDDDATDDDAAADA ' 2
•		VL.front 31-MER

FIG. 19 (42:0101)33) AATT TIL 198 H Q G L S S P V T K S F N R G E C (SELTOID: 25) DADIDIDOD TETTEAABOT DITTTETEADE DEDEABOTOA DEDOCUTEATE 61 CATCAGGGC TGAGGTCGCC CGTCACAAG AGCTTCAACA GGGGAGAGTG IJ8 T T T Z K Y D X E K H K A X Y C E A T DETECTION OF TOTAL STATEMENT STATEMENT SOLUTION OF THE STATEMENT S SOASTEARED STOOGSATST BAAASASAAA BABSATSABA SBAAASBABT SBSABTSSSA 103 SST S A L S A X S A O E A A S A O S K B S I SOURCE STORY OF TOTAGE TOTAGE TOTAGE STORY OF STORY OF THE SOURCE SOURCE STORY OF THE SOURCE SAI AACTCCCAGG AGAGTGTCAC AGAGCAGGAC AGCAAGACA GCACCTACAG CCTCAGCAGC 138 N E X B K E Y K A Ö M K A D N Y F Ö Z C ADDDATTOD ADDDDDTTAT DOADDTTDOA DITACTTO DODDTDTDD DATADAADTT 181 AACTTCTATC CCAGAGAGGC CAAAGTACAG TGGAAGGTGG AAAACTCGGGT TISE PPS DEQ LAS GTAS V U L L ATTOADOAD ACATATABA CCTTGACGAA GACAACAC GGACGACTAA TAASTOSTO STEETING TTOSTOADS TOTAASTTS ASSAGTASTS TASSESSORT ISA 98 F G P G T K L E L R R A A A A P S V F I DATABADAD DATABATOT TOTABATOT TOTABATOT ADOTTOTAL DATABATOTAL BSEBI CDK #3 78 V Q S E D L A D Y F C Q Q X N I X DETEABABEA TABATETTAT ATTECTEDADA BAAATAETST ESCARETETT SABASTESSAS 301 GTGCAGTCTG AAGACTTGGC AGACTATTTC TGTCAGCAAT ATAACATCTA TCCTCTCACG SS V P D R F T G S G T D F T L T ATOOCTOATO OTOAOAOTOA AATOTOTOCO AOATOCACTO COLORADO DATOAOODAO TADDADIAD CACTOTACT TTABADADED TOTABETEAD DEADADITED CLASTOCHE IAS CDK #5 38 OK B C OS B K Y I I X Z Z Z K K TOCADITAD DEDITABATE ADEADTAAAT DADIDITITA DEADATTECO OTESTITOTE ASSTSACATE SOCIATION TO TATACTE STORY STATEMENT STORY CDK #I \* \* \* 18 R V S V T C K A S O N V G T N V A TTDATACCA BOTACATTAD TACCACATT CTDACTEDOC TTDCAGGTDA COCTACATT 121 AGGTCAGCG TCACCTGCAA GGCCAGTCAA DATGTGGGTA CATGTAGC CTGGTATCAA -3 A Y A D I V M T Q S Q K F M Z L Z A G D STOTOOTACT DATGEDACA TOAATTTTTD ADACTOTOTO ATDACOATAT CADCOTACOO SABABBATBA STASASSTOT ASTTAAAAAS TSTASASSASTATA STSBSATBSB 18 -23 M K K N I Y E T F Y Z M E A E Z I DITTETADA ATABAAAAA DAADATADA TODAADAAAA AATODDATAT TOTTTOTTOAT I ATATATTTTT DOTTATAT ADATATAT TTADDOTATA ADAADAADIA

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**TTAA** 

### FIG. 20A

9 T S	S S d	CACCACTGGC	S S I		OTCAGGAGTC 8	BLT
DDDDTTDDAD	DADOTODOT 2T00400001	SOCIASTESTS	DDADDADTDD	OTOATOTO40	DADTDDAD I	109
A V L	L E b	DOACGCCACACA	T I A		TGCCACAGCA W S W T	351
ATOOTOTOOD	DODTTODADA DODA ADOTOT	DDTDDDDDDA DD4DDDDDA	SOMOTOSSES	<b>DDACTCAADD</b>	TECTOTODOA 1	175
E b A	K E b	GACCAGTTCC	2 9 T	and a second of the second of	TGGAGACCCC	138
STSSSSAASS SASSSTTSS	DODTTDATDA	SSAASTSSTS SSATSASSAS	SOTSESSTSS	Sesson	SSSTOTOOA 1	187
S X S	S 4 A	CAGAAGGGGG	S d D	X L S	CAGAGACGTC	118
DDADAADOTO DOTOTTDDAD	DTDDDADDT 94999T9DD4	SSSSSTATSTS	DOTACOCODE	AADDADCTOD	SADSTOTOTS 1	421
				CDK #3		
тул	бет	* * <u>*</u> <del>Z</del>	T W F	• -	<u>1 1</u> 4 7 8	86
4010477494	DESCRIPTION OF THE PROPERTY OF	SOSTANTES SOSTANTES	TACTTGGTTT ATGAACCAAA	DDDDTTDATT DDDDAADTAA	ADTDDDDADA . TDADDDDTDT	198
		Z E D L	гк	ѕ ж ŏ	TATLS	
Tecacetta A D Y	หหาหมากาม	AGACTCCT	STTSABASTS	<b>DTDATTTDDA</b>	SOATETSSSA . BETASABEET	10£
ADDTDTDATT	TTOTACORAC	4745545T7T	O V V DUDUDAD	2400444000	0012020	
					7	
			*	* * *	CDK #5	
Y K N	K D N	ADATOOTOAA 2 I T T	TODDOOTTO	TOTOTOTOD  V S G  * * *	DATAATADDT	-
กราวราคคาพ	7.7.9.7.7.7.999	ADATOUTDAA	TODDOOOTTO	TOTOTOTOD  V S G  * * *	4 * * * *	-
* * *  SAABAASSET  ETTSTEESSA	*	+ + TOTACCACTT ADATEDTOAA	ADDDDDDAAD TDDDDDDTTD	TOTOAOAOAO AOAOTOTOTO V 2 G	OTATTATODA DATAATAODT T Y Y Y T	Z # Z
S <u>Q D</u> * * *  STATISTICAL  ST	AADABABDDD	I T A V  TOTACOACT  TOTACOACT  TOTACOACT  ADATODTOAA	GACCTCAAC  L E L  GAAGGGCCGA  CATCCCGGCT  CTTCCCGGCT	S X D  CACACATCT  A A A A A A A A A A A A A A A A A A A	0A5T5T5555         q       T       Q       R         q       T       Q       R         0ATATAT55T       PATAT55T       R       R         q       Y       Y       T         q       Y       Y       T         q       Y       Y       T	38
S <u>Q D</u> * * *  STATISTICAL  ST	AADABABDDD	I T A V  TOTACOACT  TOTACOACT  TOTACOACT  ADATODTOAA	GACCTCAAC  L E L  GAAGGGCCGA  CATCCCGGCT  CTTCCCGGCT	S X D  CACACATCT  A A A A A A A A A A A A A A A A A A A	OTATTATODA DATAATAODT T Y Y Y T	38
S G S S S S S S S S S S S S S S S S S S	AADABABDDD	I# AGD ASSESSED THE	GACCTCAAC  L E L  GAAGGGCCGA  CATCCCGGCT  CTTCCCGGCT	S X D  CACACATCT  A A A A A A A A A A A A A A A A A A A	0A5T5T5555         q       T       Q       R         q       T       Q       R         0ATATAT55T       PATAT55T       R       R         q       Y       Y       T         q       Y       Y       T         q       Y       Y       T	38
DATABTEST  SOTATOADS  SOTATOADS  SOTATOADS  A A A A A A A A A A A A A A A A A A A	AATAATAATTAAATTAAATTAAATTAAATTAAAAAAAA	# AGDACOANA  T# AGD  AGACATAGA  TOPACACATAGA  TOPACACATAGA	S G F CCTGGAGTTG GGACCTCAAC L E L GAAGGGCCGA GAAGGGCCGA CTTCCCGGCT	A A D CAGGCAAGAG CAGGCAAGAG CAGGCAAGAG CAGGCAAGAG CAGGCAAGAGAGACAGAC	E I X I I I I I I I I I I I I I I I I I	7 7 7 8 7 8 7 8 7 8 7 8 7 8 7 8 7 8 7 8
V W Z  DATABTEET  DATABTEET  DATATOACO  S G D  TABAAACOET  DAABAACOET  DAABAACOET  DAABAACOET  DAABAACOET  DAABAACOET	M D X  * * * * * * * * * * * * * * * * * *	TACTEAATAT  2	SAGACCTAAG  S G F  CCTGGAGTTG  GAAGGGCCGA  GAAGGGCCGA  CTCCCGGCT  CTCCCGGCT  CTCCCCGCT	A A D  CAGGCAAGAG  CAGGCCAAGAG  C	E I X I I I I I I I I I I I I I I I I I	177 88 181
TTOOOTTOTE  AACCOMAGAC  V W Z  CONTRACTOOT	TADSSTATTS ATSCHOOL AT STATE AT STATE AT	ATCACATA  TATACACTA  TATACACTA  TATACACATA  TATACACACA  TATACACATA  TATACACATA	V E S  CTCTGGATTC GAGACCTAAG S  CCTGGAGTTG GGACCTCAAC L E L L E L L E A  CAAGGGCCGA  GAAGGGCCGA  CAAGGGCCGA  CAAGGGCCGA  CAAGGGCCGA  CAAGGGCCCAA  CAAGGGCCCAA  CAAGGGCCCAA  CAAGGGCCCAA  CAAGGGCCCAA  CAAGGGCCCAA  CAAGGGCCCAA  CAAGGCCCCAA  CAAGGCCCCCAA  CAAGGCCCCCCAA  CAAGGCCCCCCAA  CAAGGCCCCCCAA  CAAGGCCCCCCCAA  CAAGGCCCCCCAA  CAAGGCCCCCCAA  CAAGGCCCCCCAA  CAAGGCCCCCCCAA  CAAGGCCCCCCCAA  CAAGGCCCCCCCAA  CAAGGCCCCCCCC	V Q L CCTGTGCAGC GGACACGTGC CAGGCAAGAG GTCCGTTCTC GTCTGTTCTC GTCTGTTCTCT GTCTGTTCT GTCTGTT GTCTGTTCT GTCTGTTCT GTCTGTTCT GTCTGTT GTCTT GTCTGTT GTCTT GTCT GTCT GTCT GTCT GTC	A Y A A A A A A A A A A A A A A A A A A	177 88 181 81
E DESCRIPTION OF THE PROPERTY	4 4 V  TADSSTATE  TADSSTATE  ATSCH  A D  TADSSTATA  A D  TATATAATA  TATATATAA  TATATATAA  AADASSSSS  AADASSSSS  TATATOTOSS	A DO STANDARD A DE SERVICIO AT DA	V E S  CTCTGGATTC GACCCTAAG GACCCTCAAG GCACCTCAAC GGACCTCAAC GGACCTCAAC GGACCTCAAC GGACCTCAAC T E L  GAAGGGCCGA CTTCCCGGCTT	TCCACGTCGA V Q L CCTGTGCAGC GGACACGTCG CAAAA CAGGCAAGA CAGGCAAGA CAGGCAAGA CAGGCAAGA CAGGCAAGA CAACACTCTC CAGGCAAGA CAACACTCTC CAGGCAAGA CAACACTCTC CAGGCAAGA CAACACTCTC CAGGCAAGA CAACACTCTC CAGGCAAGA CAACACTCTC CAGGCAAGA CAACACTCTCACA CAACACTCTCACA CAACACTCACACA CAACACTCACACA CAACACTCACACA CAACACTCACACACA	A Y A A A A A A A A A A A A A A A A A A	177 88 181 171 8-
DOTES OF THE PROPERTY OF THE P	T 2 4 C 5050507074 C 6050507074 C 7 4 V C 7 4 V C 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7	TODE ADDED SO TO A T	A L L L A CONTRACT CACCTCAGA V E S V CTCTGGATTC GAGACTTGGAGTTG GAGAGTTG GAAGGGGCCGA CTTC CAGGGCCGA CTTC CAGGGCCGA CTTC CAGGGCCGA CTTC CAGGGCCGA CTTC CAGGGCCGA CTTC CTTC	T A I AGTGCAGCT ACCACGTGA  Y Q L OUT COTGTGCAGC GACACGTCG A A C CAGGCAAGAG CACACGTCT CACGCCAAGAG A A C CACGCCAAGAG CACACGTCT CACAC	M K K N GEGTACGCTG CGCATGCGAC A Y A E A Y A E CTGAAACTCT CACAACTCT CACACACACACACACACACACA	177 88 181 171 8-

### FIG. 20B

721 GTTGAGCCCA AATCTTGTGA CAAAACTCAC ACATGA (SEQ IONO: 26)
CAACTCGGGT TTAGAACACT GTTTTGAGTG TGTACT
CAACTCGGGT TTAGAACACT GTTTTGAGTG TGTACT

CAACTCGGGT TTAGAACACT GTTTTGAGTG (SEQ IONO: 26)

661 ACCCAGACCT ACATCTGCAA CGTGAATCAC AAGCCCAGCA ACACCAAGGT GGACAAGAA TGGGTTCCA TGGGTTCA TGGGTTCCA TGGGTTCCA TGGGTTCCA TGGGTTCCA TGGGTTCA TG

## ILIGATE Chain Primers: S. CAGTCCAACTGTTCAGGACGCC 3. (SEG IO NO:1) MKLC-2, 22mer S. GTGCTGCTCATGTTGTGAGTGC 3. (SEG IO NO:2) Heavy Chain Primers: S. GCATCCTAGAGTCACGAGGAGCC 3. (SEG IO NO:3) S. GCATCCTAGAGTCACGAGGAGCC 3. (SEG IO NO:3) S. GCATCCTAGAGTCACGAGGAGCC 3. (SEG IO NO:3) S. GCATCCTAGAGTCACGAGGAGCC 3. (SEG IO NO:5) S. GCATCCTAGAGTCACGAGGAGCC 3. (SEG IO NO:5) S. GCATCCTAGAGTCACGAGGAGAGCC 3. (SEG IO NO:5)

(SEC ID NO: (P)

FIG. 21

S CGACAGCTGGGAAGGTGTGC 3'

```
Heavy chain forward primer

5. CAAACGCGTACGCT GAG ATC CAG CTG CAG CAG 3. (SELLARS)

Heavy chain reverse primer

5. CAAACGCGTACGGGTGTGTTTTGGC 3. (SELLARS)

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A A G	K B Y	E r			Ð			F	T	7	_	A V ) V		86
ADDTDDTAD1 TDDADDATDA	r Seessaaast A esseetttsa	DDAD:	OTODAA DADOTT	SAS	DDT:	DDT DDA	552	TTD:	TCAC	29	SST	TOT	AD	198
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DFT	T D S	o s	5 S	F	Я	a	ď	Λ	5 S	* S				85
ADADTTTAD/ TDTDAAATDI	A SABBBASTAB T STSSSTBATS	DTDA: DADT:	DDDTDA DDDADT	DTT:	DAD, DTD	ADA TOT	222	TDD:	DDTD DDAD	TT	TTA	922	AΑ	241
CDR #2													*	
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3	ADTTOBBBBT :	DOBAADTADT D	DASTCTGAG	OTDADDADD T	SASTTABA E	06

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Mutagenesis Primer for 6G425VL

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		A75	FIG. 2		
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<b>DDAAADTTTD</b>	AGGACTAGAT Y I J	<b>AGAGGTTTOD ADA</b>	CGGTCCGGTC	TGGACGTCTT	TOOTTACATT 181 ACCATOTAA Y W H J 85 * *
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ATTTOTADOA	ATADAAAAAA	<b>DDAADATADA</b>	TODAADAADA	AATƏDƏATAT 1	I ATGAAGAAGA TACTTCTTCT A X X W ES-

661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA CGGACGCTTC AGTGGGTAGT CCCGGACTCG AGCGGGCAGT GTTTCTCGAA GTTGTCCCCT 198 A C E V T H Q G L S S P V T K S F N R G

721 GAGTGTTAA (SEQ LØ NO: 41) CTCACAATT 218 E C O (SEQ LO NO: 42) FIG. 27B

		<b>A8</b> S	FIG.			
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STITISTADSA ATABAAAAA SSAASATABA TSSAASA AATSSATAT TSTITTTTG I ATGAAAAAA TATOTTTTTT TCTTTGCA TCTATGTTTT TGCTACAAAC

198 721 AAGAAAGTTG AGCCCAAATC TTGTGACAAA ACTCACACAT GA 661 TTGGGCACCC AGACCTACAT CTGCAACGTG AATCACAAGC CCAGCAACAC CAAGGTGGAC AACCCGTGGG TCTGGATGTA GACGTTGCAC TTAGTGTTCG GGTCGTTGTG GTTCCACCTG L G T Q T Y I C N V N H K P S N T K V D TTCTTTCAAC TCGGGTTTAG AACACTGTTT TGAGTGTGTA CT (SEQ ID NO: 43)

FIG. 28B

218 K K V E

CDK

THTO

(SER SD NO: 44)

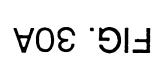
### Variable Light Chain Domain

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VSNRFSGVPSRFSGSGSGTDETLTISSLQPEDFATYYCSQSTHVPLTFGQGTKVEIKR (5EQ ID AC:44)	F(ab)-1 YK
VSNRFSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCSQSTHVPLTFGQGTKVEIKR (SEQ ID AC: 45)	E(8P)-1 XK
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SHIT GEPSELSAGDRYTITCRSSGSLVHGIGNTYLHWYQQKPGKAPKLLIY   (SEL I) LO: 40 100  (SEL I) LO: 45)  WHIT SPESSELSAGDRYTITCRSSGSLVHGIGNTYLECKSTRULLK   # ################################	E(8p)-1 XE 20 20 20 20 20 20 20 20 20 20 20 20 20
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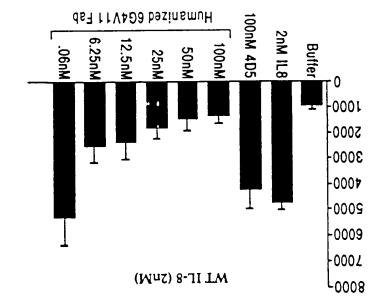
**EIG. 29** 

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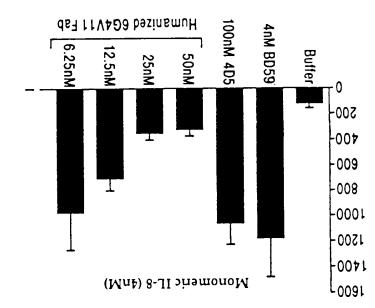


IC20~12nM



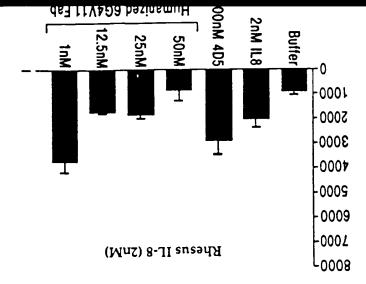
### **EIG. 30B**

IC20~12uM





IC20~55uM



# Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11 Light Chain

EC (SEQ ID NO: 51) ALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG MKKNIAFLLASMFVFSIATNAYADIQMTQSPSSLSASVGDRVTITCRSSQSLVHGIGNTY HVPLTFGQGTKVEIKRTVAAPSVFTFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN LHWYQQKPGKAPKLLIYKVSNRFSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCSQST

### Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11 Heavy Chain

WVRQAPGKGLEWVGYIDPSNGETTYNQKFKGRFTLSRDNSKNTAYLQMNSLRAEDTAVYY MKKNIAFLLASMFVFSIATNAYAEVQLVQSGGGLVQPGGSLRLSCAASGYSFSSHYMH CARGDYRYNGDWFFDVWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF VDKKVEPKSCDKTHT (SEG ID NO: 5'Z) PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTK

## Amino Acid Sequence of the peptide linker and M13 Phage Coat (gene-III)

GLANGNGATGDFAGSSNSQMAQVGDGDNSPLMNNFRQYLPSLPQSVECRPFVFSAGKPY SGGGSGSGDFDYEKMANANKGAMTENADENALQSDAKGKLDSVATDYGAAIDGFIGDVS EFSIDCDKINLFRGVFAFLLYVATFMYVFSTFANILRNKES (5E0 10 No: 53)

### FIG. 31A

FIG. 31B

1ST GAGTGTTAAG CTGATCCTCT ACGCGGACG CATCGTGGCC CTAGTACGCA ACTAGTCGTA (紀公本 137) CTCACAATTC GACTAGAGACA TGCGGACG TGCGGACA TGCGACA TGCACA TGCGACA TGCACA TGCACA TGCCACA TGCCACA TGCGACA TGCGACA TGCACA TGCACACA TGCACACA TGCACACA TGCACA TGCACACA TGCACACA TGCACACA TGCACACA TGCACACA TGCACACA TGCACACA TGCACACA TGCACACA

- 661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGAA CGGAACTC AGTGGGTAACT CCGGGAACTC AGTGGGGAACTC AGTGGGAACTC AGTGGGAACTC AGTGGGAACTC AGTGGGAACTC AGTGGGAACTC AGTGGGAACTC AGTGGAACTC AGTGAACTC AGTGGAACTC AGTGGAACTC AGTGGAACTC AGTGGAACTC AGTGGAACTC AGTGAACTC AGTGGAACTC AGTGGAACTC AGTGGAACTC AGTGGAACTC AGTGGAACTC AGTGGAACTC AGTGGAACTC AGTGGAACTC AGTGGAACTC AGTGAACTC AGTGAACTC
- 601 TACAGCCTCA GCAGCACCCT GACGCTGAGC AAAGCAGACT ACGAGAAACA CTATCAGATG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG GTTTCAGATG
- 541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC CGGGAGGTTA GCCCATTGAG GGTCCTCTCA CAGTGTCTCG TCCTGTCGTT CCTGTCGTGG 158 Å L Q S G N S Q E S V T E Q D S K D S T
- 481 GTGTGCCTGC TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAG CACACGGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG 138 V C L L N N F Y P R E A K V Q W K V D N

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- 181 TTACACTGGT ATCAACAGAA ACCAGGAAAA GCTCCGAAAC TACTGATTTA CAAAGTATCC AATGTGACCA TACTGATTTA TGGTCCTTTT CGAGGCTTTG ATGACTAAAT GTTTCATAGG S L H W Y Q Q K P G K A P K L L L Y K V S
- TABOGGETC TOTOCOCTG TOTOCOCCTC TOTOCCTC TOTOCCT

### Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V19 Light Chain

ALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG HVPLTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN LHWYQQKPGKAPKLLIYKVSNRFSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCSQST MKKNIAFLLASMFVFSIATNAYADIQMTQSPSSLSASVGDRVTITCRSSQSLVHGIGNTY EC (SEQ ID NO: 51)

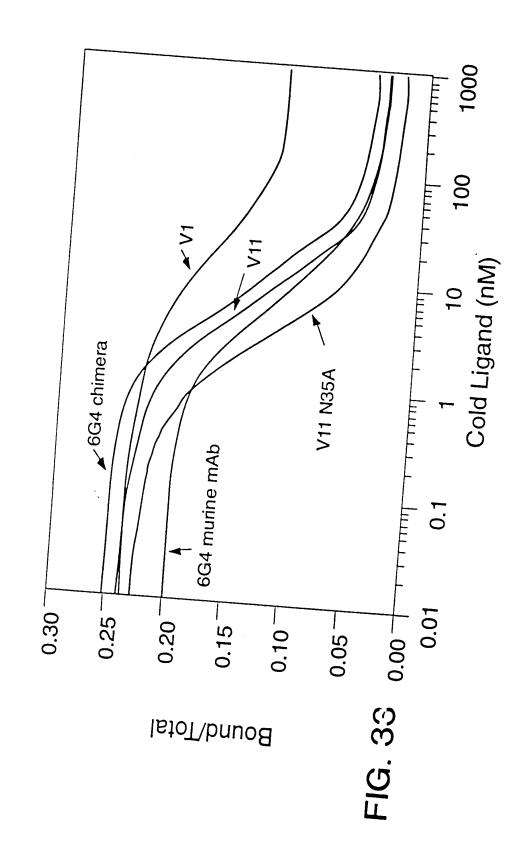
## Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V19 Heavy Chain

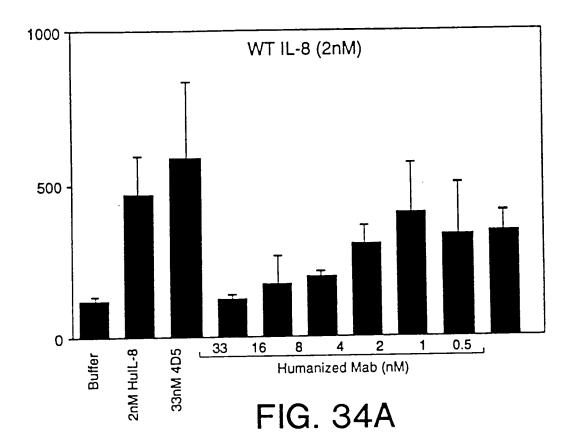
MKKNIAFLLASMFVFSIATNAYAEVQLVESGGGLVQPGGSLRLSCAASGYSFSSHYMH VDKKVEPKSCDKTHT (SEQ 10 NO: 55) CARGDYRYNGDWFFDVWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF  ${\sf WVKQAPGKGLEWVGYIDPSNGETTYNQKFKGRFTLSRDNSKNTAYLQMNSLRAEDTAVYY}$ PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTK

FIG. 31C



F16. 32





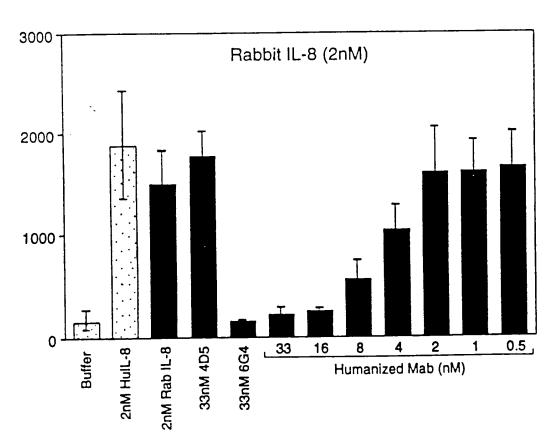
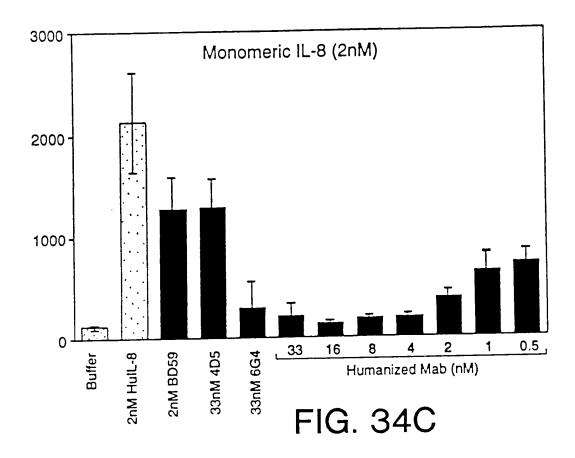
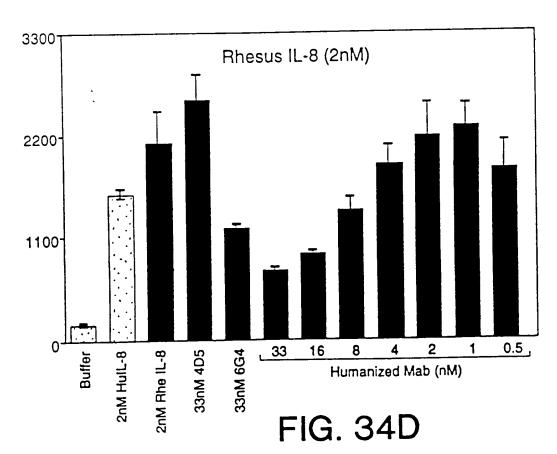


FIG. 34B





# Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11N35A Light Chain

MKKNIAFLLASMFVFSIATNAYADIQMTQSPSSLSASVGDRVTITCRSSQSLVHGIG**A**TY LHWYQQKPGKAPKLLIYKVSNRFSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCSQST HVPLTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN ALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG EC (SEQ ID NO: 56) anti-IL-8 6G4.2.5V11N35A Heavy Chain Amino Acid Sequence of the humanized

PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSSLGTQTYICNVNHKPSNTK WVRQAPGKGLEWVGYIDPSNGETTYNQKFKGRFTLSRDNSKNTAYLQMNSLRAEDTAVYY CARGDYRYNGDWFFDVWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF MKKNIAFLLASMFVFSIATNAYAEVQLVQSGGGLVQPGGSLRLSCAASGYSFSSHYMH VDKKVEPKSCDKTHT (5EQ TO M:52 Amino Acid Sequence of the putative Pepsin Cleavage Site and GCN4 Leucine Zipper

CPPCPAPE<u>LL</u>GGRMKQLEDKVEELLSKNYHLENEVARLKKLVGER (5E4ID No:57)

FIG. 35

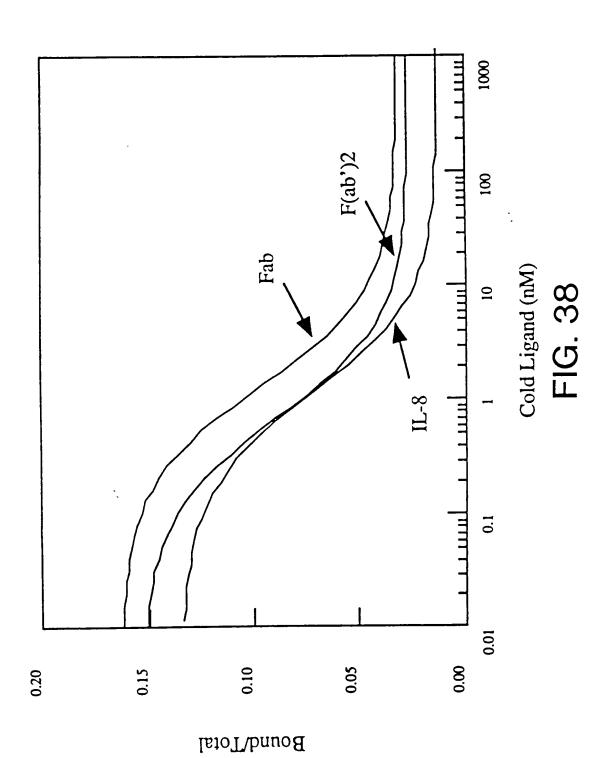
1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTCG TTTTTTCTAT TGCTACAAAC -23 M K K N I A F L L A S N AAAAAAGATA ACCAAAC
TACTTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG  -23 M K K N I A F L L A S M F V F S I
-23 M K K N I A F L L A S M F V F S I A T N  CGTATGCGAC TATACCAGAT GACCCAGTCC CCCAGGGGAC  CGTATGCGAC TATACCAGAT GACCCAGTCC CCCAGGGAC  CGTATGCGAC TATACCAGAT GACCCAGTCC CCCAGGAC  CGTATGCGAC TATACCAGAT GACCCAGTCC CCCAGGCAC  CGTATGCGAC TATACCAGAT GACCCAGTCC CCCAGGCAC  CGTATGCGAC TATACCAGAT GACCCAGTCC CCCAGGCAC  CGTATGCGACACAGAC  CGTATGCGACACACACACACACACACACACACACACACAC
N I A F I AGATACAAGC AAAAAC
61 GCATACGCTG ATATCCAGAT GACCCAGTCC CCGAGCTCCC TGTCCGCCTC TGTGGGCGAT  -3 A Y A D I Q M T Q S P S CAAAAAAGATA ACGATGTTTG  61 GCATACGCTG ATATCCAGAT GACCCAGTCC CCGAGCTCCC TGTCCGCCTC TGTGGGCGAT  121
Company Translation of the Company o
CGTATGCGAC TATAGGTCTA CTGGGTCAGG GGCTCGAGGCTCCC TGTCCGCCTC TGTGGGCGAT  -3 A Y A D I Q M T Q S P S S L S A S V G D  121 AGGGTCACCA TCACCTGCAG GTCAAGTCAA AGCTTAGTAGT
A D I O T CTGGGTCAGG GGCTCGACGC TGTCCGCCTC TGTCGCCCTC
T Q S P C ACAGGCGGAG ACAGGCGGAG
121 AGGGTCACC.
TCCCC CMCCC CMCCC
18 R V T T T T T T T T T T T T T T T T T T
121 AGGGTCACCA TCACCTGCAG GTCAAGTCAA AGCTTAGTAC ATGGTATAGG TGCTACGTAT  18 R V T I T C R S S O S I TACCATATCC ACGATGTAT
181 TTLCACMORA
A A MOON
38 L H W Y Q Q K P G K A P K L L I Y K V S
W Y Q Q K B CONTINUE OF A CANAGTATIC
241 ANTONIA
TATIOGATICT CTGGAGTCCC mmo-
TAGCTAAGA GACCTCACCO TTCTCGCTTC TCTCGCATCCC
241 AATCGATTCT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC GGATTTCACT  TTAGCTAAGA GACCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCCTG CCTAAAAT GTTTCATAGG  S8 N R F S G V P S R F S CTAGGC CAAGACCCTG CCTAAAAT GTTTCACT
S R F S C TAGGC CAAGACCCTG CCTALLACT
TTAGCTAAGA GACCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCCTG CCTAAAGTGA  301 CTGACCATCA GCAGTCTGGA  TTCTCGCTTC TCTGGATCCG GTTCTGGGAC GGATTTCACT  S G S G S G S G T D AAGAGCGAAG GGATTTCACT
GACTOON COOLS
301 CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTTC ACAGAGTACT  78 L T I S S L Q P E D F T TACTGTAGA TATTGACAAG TCTCTGAACTT
S L Q P E D AAGCGTTGAA TAATGACAA ACAGAGTACT
301 CATCHOORS
GTACACO TOTAL TOTAL TOTAL ACACOCO
98 H V D AGTGCAAACC TGTCCCATCC
361 CATGTCCCGC TCACGTTTGG ACAGGGTACC AAGGTGGAGA TCAAACGAAC TGTGCTCATGA GTACAGGGCG AGTGCAAACC TGTCCCATGG TTCCACCTCT AGTTTGCTTG ACACGCTGCA  98 H V P L T F G Q G T K V
*21 CCATCTOTOTOTO
Company of the Compan
GGTAGACAGA AGTAGAAGGG CGCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT  118 P S V F I F P P S D E Q L K S G T A S V  CACACGGACG ACTINATION TO TATCCCAGA GACCAGA GACCAGA CACAGGACG ACTINATION TO TATCCCAGA GACCAGA CACAGGACG ACTINATION TO TATCCCAGA GACCAGA CACAGGACG ACTINATION TO TATCCCAGA GACCAGA GACCAGA CACAGACGA CACAGGACG ACTINATION TO TATCCCAGA GACCAGA GACCAGA CACAGACGA CACAGACA CACAGACA CACAGACGA CACAGACA CACAGACA CACAGACA CACAGACACA CACAGACACACA CACACAGA CACAGACA CACAGACACA CACAGACACA CACAGACACA CACAGACACA CACAGACACACA CACAGACACA CACAGACACACA CACAGACACACAC
F I F P D TAGACTA CTCGTCAACT TTCGGAAC TGCTTCTGTT
481 GTCTCCCC
481 GTGTGCCTGC TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC  CACACGGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG  138 V C L L N N F Y P R E A K V Q W K V D N  CGGGAGGTTA GCCCATTGAA CCCAGGAGAGT GTCACACACACACACACACACACACACACACACACACACA
L L N N E GATAGGGTCT CTCCGGTTTC
P R E A V T ATGTCACCTT CCACCTAME
SAL GCCCTCCAAT CGGGTAACH
CGGGAGGTTA GCCCATTOL CCAGGAGAGT GTCAGAGAGAGT
541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC CGGGAGGTTA GCCCATTGAG GGTCCTCTCA CAGTGTCTCG TCCTGTCGTT CCTGTCGTGG  601 TACAGCCTCA GCAGCAGGA
N S Q E S V TOTAL TOTAL GOALAGCACC
601 TACACCOMO
A MOME - CANOCAL ( TYP CANOCE - CANOCAL )
178 Y S L CGTCGTGGGA CTGCGACTCC AAAGCAGACT ACGAGAACA
601 TACAGCCTCA GCAGCACCCT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC  178 Y S L S S T L T L S K A D Y E K H K V Y  661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCCCCCCCC  662 GCCTTC ACTCCCCATCA GGGCCTGAGC TCCCCCCCCCC
OUT GOODS -
COOL - TO A COOL -
198 A C AGTGGGTAGT CCCGGGGGG TCGCCCGTCA CARACTOCT
661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA  198 A C E V T H Q G L S S P V T K S F M S T T CACCCTT T T T T T T T T T T T T T T
721 GLOTOTTO
198 A C E V T H Q G L S S P V T K S F N R G  CTCACAATTC GAGTICTCT ACGCCGGACG CATGORDS  CTCACAATTC GAGTICTCT ACGCCGGACG CATGORDS
218 F. GACTAGGAGA TECCEGGACG CATCGTGGCC CTT-
218 E C O (SEQID NO: 56)  TGCGGCCTGC GTAGCACCG GATCATGCCTA ACTAGTCGTA (SECIDALISE)
The state of the s
FIG. 36
114.36
- <del>-</del>

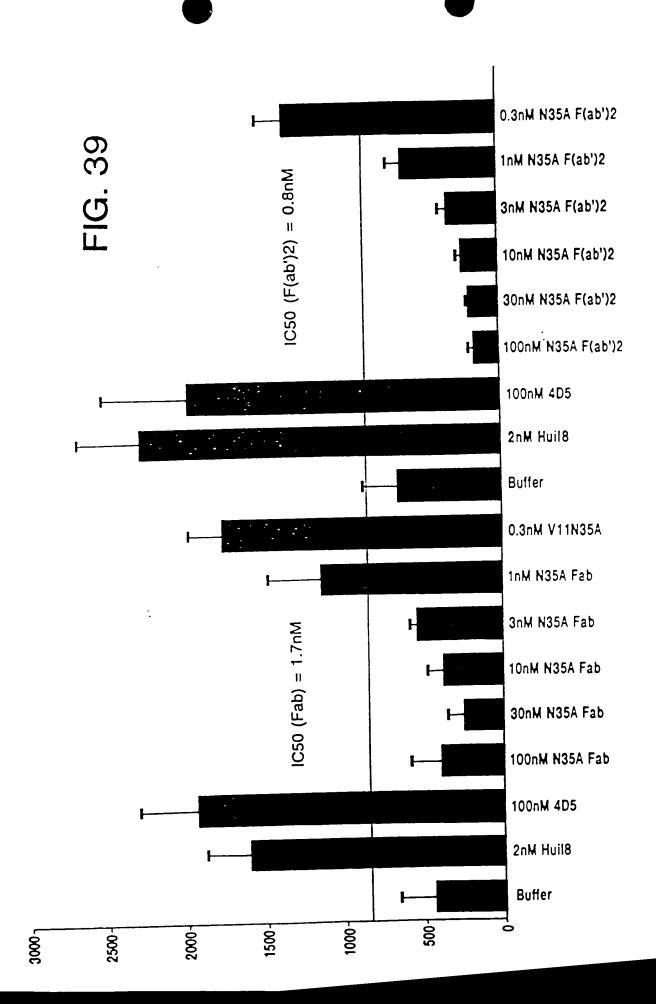
781	AAA	AGC	GT	ΤA	CTAG	AGG'	TTG	AGGT	rga:	TTTT	ATC	AA	\AAG	A	ATAT	CGC	ATT	TCTT	'CTT	GCA
-1		TCC	CA	TA	GATC	TCC.	AAC	TCC	ACTA	AAAA	M M	K	K	N	ATAT I	A	F	L	L	A
	AGA	TAC	AA"	GC	AAAA	AAG	ATA	ACG!	ATG'	TTTG	CGC	TAC	GCGA	7C	AGGT TCCA	AGT	CGA	TCAC	GTC	AGA
-11	S	M	F	v	F	S	I	A	T	N	Α	Y	A	Ε	V	Q	L	V	Q	S
	CCG	CC	700	25	ACCA	CGT	CGG	TCC		GAGT	GAC	3GC/	AAAC	:A	CCTG GGAC	ACG	100	AAGA	1000	MIG
	G	G	G	L	V	Q	P	G	G	S	L	R	L	S	С	A	Α	5	<u>. L.</u>	
961	TCC	TT	CTC	GA	GTCA	CTA	TAT	GCA	CTG	GGTC	CG	rca(	GGC	CC	CGGG	AAT TT 4	GGG	CCTC	GAA	ATGG PACC
28	AGG S	AA( F	GAG S	CT S	CAGI H	GAT Y	'ATA <u>M</u>	CGT	GAC W	V	R	Q Q	A	P	GCCC G	K	G	L	E	W
1021																				CCGT
	CAA	CC'	TAT	TАT	AACT	rAGG	AAG	GTT	ACC	ACTT	TG	ATG	CATA	$\mathbf{T}_{\mathcal{F}}$	TAGT	TTT	CAA	GTT		JGCA
48	V	G	<u>Y</u> _	I	D	P_	<u>_S_</u>	_N_	_G_	E	T	<u>T</u>	<u>_Y_</u>	N	0_	_K_	_F	K	<u>G</u>	R
1081	TTC	'AC'	TTI	TAT	CTCC	GCGA	CAA	CTC	CAA	AAAC	AC.	AGC	ATA	CC	TGCA	GAT	GAA	CAG	CCT	GCGT
60					GAG(			GAG S	GTT K	TTTG N	TG' T	TCG <b>A</b>	TAT( Y	GG L	ACGT Q	M M	N	S	L L	R
1141	GCT	GA	GGA	ACA	CTG	CGI	CTA	TTA AAT	CTG	TGCA	AG TC	AGG TCC	GGA'	AA.	TAGO	GA7	CAA TGTT	ACC	ACT	GACC
88	A	E	D.	T	A	V	Y	Y	С	A	R	G_	_D_	Y	R	<u>Y</u>	N	G_	_D_	_W
1201	TTC	TT	CGI	ACG	TCT	GGG	STCA	AGG	AAC	CCTG	GT	CAC	CGT	СТ	ССТО	CGG	CTC	CAC	CAA	GGGC
	ממ	A A	GC	rgc	AGA	ccc	CAGT	TCC	TTC	GGAC	CA	GTG	GCA	GA	GGA(	3CCC	<b>JGAG</b>	GIG	GTT K	
1261	CCZ	ATC	GG'	TCT	TCC	CCC	rggc Necc	ACC	CTC	CTCC	<b>А.А</b> : тт :	GAC CTC	CAC GTG	CT GA	CTG(	GGG(	GCAC CGTG	AGC TCG	CCG	GGAC
128	P	S	V	AGA T.	P	JGG/	A	P	S	S	K	S	T	S	G	G	T	A	A	L
1221	CC/	-mc		TCC	ጥርአ	NGG:	מ תרט <i>ב</i>	רייי		CGAA	CC	GG1	GAC	GG	TGT	CGT	GGAA	CTC	AGG	CGCC
	CCC	220	CC	200	AGT	TCC'	TGAT	' GAA	\GG(	GCTI	'GG	CCA	$\Lambda$ CTG	CC	ACA	JCA(		GAG	ICC	GCGG
148	G	С	L	V	K	D	Y	F	P	E	P	V	Т	V	S	W	N	5	G	A
1381	CT	GAC	CA	GCG	GCG	TGC.	ACAC	CTI	rcc	CGGCI	GI	CCI	CACA	GT	CCT	CAG	GACT	CTA	OTO	CCTC
160	GA	CTC	GT	CGC	CGC	ACG'	TGTC T	GA/ F	AGG( P	GCCG <i>F</i> A	V. CA	IGGA L	ATGT Q	CA S	S CGA	GTC(	CIGA L	. GAI Y	S	GGAG L
	TC	CTC	300	ACC	י ארת	CGC	ACGC	GAC	GGT	CGTC	3 AA	/CC	CGTG	;GG	TCT	GGA	1617	GAC	.Gli	CGTG
188	s	S	٧	v	T	v	P	s	s	S	L	G	T	Q	T	Y	I	С	N	v
1501	AA	TC	\CA	AGC	CCA	.GCA	ACAC	CA	AGG'	TCGA	C AJ	AGA.	AAGI	TG	AGC	CCA	TAA	TTC	TGA	CAAA
	بالسال	z.cr	гст	TCG	GGT	CGT	TGTO	GT	TCC.	AGCT	3 T.	$\Gamma C T'$	TTCA	\AC	TCG	GGT	TTAC	JAAL	ACI	.GIII
																				K
1561	L AC	TC	ACA	CAT	GCC	CGC	CGT	CC	CAG	CACC	A G	AAC' TTG	TGCT ACGZ	rGC	GCG CGC	GCC CGG	GCA:	r GAZ A CTI	LACA LTG:	AGCTA CGAT
228	TG 3 T	AG' H	IGI T	C TA	: E	) P	C	P GG	A	P	E	L	L		G	R	M	K	Q	L
										IG										
									1	I	• '			1						

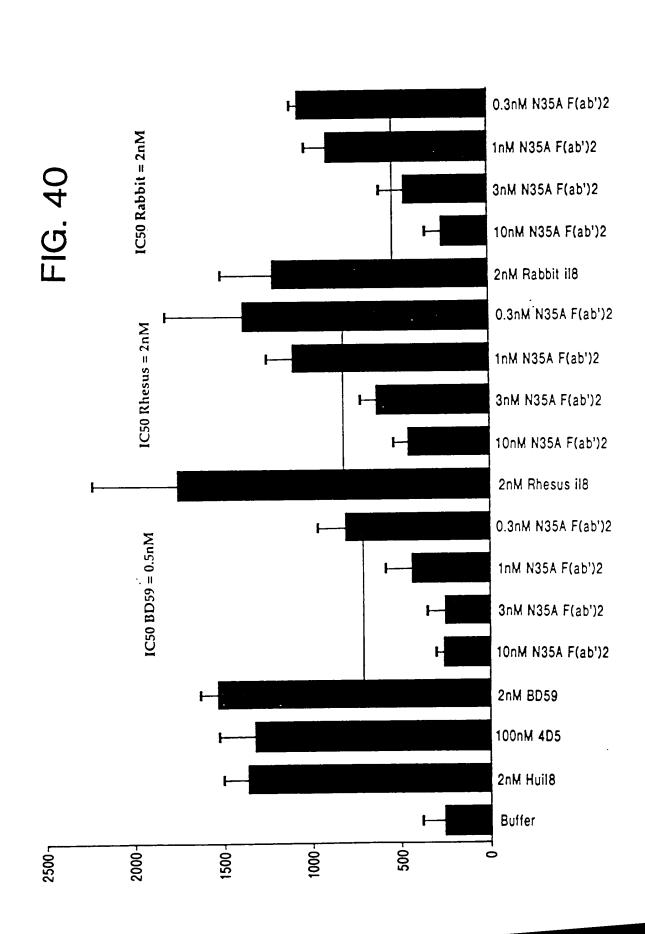
1621 GAGGACAAGG TCGAAGAGCT ACTCTCCAAG AACTACCACC TAGAGAATGA AGTGGCAAGA CTCCTGTTCC AGCTTCTCGA TGAGAGGTTC TTGATGGTGG ATCTCTTACT TCACCGTTCT 248 E D K V E E L L S K N Y H L E N E V A R

1681 CTCAAAAAGC TTGTCGGGGA GCGCTAA (SEG ID NO: 59)
GAGTTTTCG AACAGCCCCT CGCGATT
268 L K K L V G E R O (SEG ID No: 60)

FIG. 37B







#### FIG. 41A

pleI mboII taqI earI/ksp632I mboII hinfI AAAAAGAAGAAGTCGAAT TITITICITCT TCTCAGCTTA	sau3AI mbol/ndeII[dam-] dpnI[dam+] dpnII[dam-]  bclI[dam-] mnlI GTTGATTGAT CAGGTAGAGG	mnlI fokI sfaNI GCATC CTCGTCAGTA CGTAG GAGCAGTCAT	alul ssti saci saci hqiJII hqiJII hqiAI/aspHI ec1136II ecORI bsp1286 rmaI bsiHKAI maeI bmyI bfaI taqI maeIII apol banII GTAACTA GAATTCGAGC
aluI mboII taqI hindIII mboII taqI txu9I cac8I cac8I mboII hinfI carI/Ksp632I mseI cac8I mboII hinfI carCAACAATAAA TTCGAACGGG TTTTCTTCT TCTCAGCTTA	acil nspbil ACCAACAGG	a TTGAAG	tru9I mae rt tttaatgta tttgta
ddeI bsrDI TCATTGCTGA GTTGTTATT AGTAACGACT CAACAATAA	hinpi hhai/cfoi TCGCAATATG GCGCAAAATG AGCGTTATAC CGCGTTTTAC	thal fuudHI bsoFI bbvI maeII fuudHI stUI snaBI bsoFI bsh1236I bbvI hinPI bsaAI aluI hhal/cfoI GAGCTGCTGC GCGAATTACGT AAAGAAGTTA	pali III/eclXI ahdi/eam11051 mAi GACTT ATAGTCGCTT TGTTTTAT
nlaiii AAATACAGAC ATGAAAAATC TTTATGTCTG TACTTTTTAG	msli maeili bgrDi KTTATCGTCA CTGCAATATG	bsmI GCATTCCTGA CGACGATACG	haeIII/pali mcri eagl/xmaIII/eclXi eagl/xmaIII/eclXi cfri b5fri maeIII b5mAI maeIII maeIII AGTIGTCACG GCCGAGACTT ATAGTCGCTT TGTTTTTATT TTTTAATGTA TTTGTAACAT TCAACAGTGC CGGCTCTGAA ACAAAAAAAAAAAAAAAA
ecori pfimi apoi bsli GAATTCAACT TCTCCATACT TTGGATAAGG /	bspMI hinPI hhal/cfol hhal/cfol aluI avill/fspI hindili crtGAACTGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATATG CTTGACACAC GCGTCCATGT TCGAAACCTC TAATAGCAGT GACGTTACA AGCTTATAC	mbli sfani GAGGTAAAG CCCGATGCCA	haeIII/pali mcri eagl/xmaIII/eclXI eagl/xmaIII/eclXI eal pvuli cfri pvuli bsiEI ahdI/eam11051 tru9I bfal maeIII bsmAI  CTTTTCAACA GCTGTCATAA AGTTGTCACG GCGGAGACTT ATAGTCGCTT TGTTTTAATGTA TTTGTAACTA GAAAAGTTGT CGACAGATT TCAACAGTGC CGGCTCTGAA TATCAGGGAA ACAAAAATAACAT AAACATTGAT
ccori apoi 1 Gaattcaact t Cttaagtga a	bs hinPI hhal/ mstI avill/ 101 GAACTGTGTG CGC CTTGACACAC GCG	rsal hinpi hhal/cfol mnli haeli csp61 201 GGCGCTGTA CGAGG	tru9I mBeI 101 AAAAGITAAT C

!

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AGCCATGGGC CCCTAGGAGA GCTCCAACTC CACTAAAATA CTTTTTCTTA TAGCGTAAAG AAGAACGTAG ATACAAGCAA AAAAGATAAC GATGTTTGCG
M K K N I A F L L A S M F V F S I A T N A
                                                                                                                                                                                                                                                                                                                                                                            401 TCGGTACCCG GGGATCCTCT CGAGGTTGAG GTGATTTTAT GAAAAAGAAT ATCGCATTTC TTCTTGCATC TATGTTCGTT TTTTCTATTG CTACAAACGC
                                                                                                                                                                                                                                                                                                                                                                                                                a mutation was found that inactivated the mluI site. The penultimate nucleotide was changed fr G toT ^{\circ}
                                                                                                                                                                                                                                                                                                                                                                 mboli sfani
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  hgiJII
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   saci
                                                                                                                                                                                                                                                                                                                                                   hphI
                                                                                                                                                                                                                                                                                                                                                                  alwi[dam-] muli muli
                                                                                                                                                                                                                                         mbol/ndeII[dam-]
                                                                                                                                                                                                                                                                          nlaIV paeR7I
                                                                                                                                                                                                                      sau3AI taqI
                                                                                                                                                                                                                                                                                            kpnI cauII dpnII[dam-]
                                                                                                                                                                                                                                                          dpnI[dam+]
                                                                                                                                                                                                                                                                                                                batYI/xhoII
                                                                                                                                                                                                                                                                                                                                  bani bsaJi alwi[dam-]
                                                                                                                                                                                                                                                                                                                                                    bamHI avaI
                                                                                                                                                                                  xhoI
                                                                                                                                                                                                    mnlI
                                                                                         xmaI/pspAI
                                                    hpaII
BCrFI
                                                                       dsav
                                                                                                                                                                                  Caull
                                                                                                                             SCIFI
                                                                                                                                                                                                     bsaJI
                 ncil
                                   Idem
                                                                                                            gma I
                                                                                                                                              nciI
                                                                                                                                                                dsaV
                                                                                                                                                                                                                       avaI
                                                                                                                                                                                                                                                                                                                                                     asp718
                                                                                                                                                                                                                                                                                                                                                                       acc651
                                                                                                                                                                                                                                                            csp6I
                                                                                                                                                                                                                                           rsaI
                                                                                                                                                                                                                                                                             nlaIV
                                                                                                                                                                                                                                                                                                                  hqici
```

FIG. 41B

INTECCACTA INGGICTACT GGGICAGGGG CICGAGGGAC AGGCGGAGAC ACCCGCIAIC CCAGIGGIAG IGGACGICCA GIICAGIIIC GAAICAIGIA 01 ATACGCTGAT ATCCAGATGA CCCAGTCCCC GAGCTCCCTG TCCGCCTCTG TGGCCGATAG GGTCACCATC ACCTGCAGGT CAAGTCAAAG CTTAGTACAT

SASV

SSL

I O M T

TCRS

ddel nlaili

sse8387I

bspMI

maelll

molI acil

bsrI avaI aluI tth1111/aspI banII

ecoRV

bmyI

DSmFI

pstI scfI

bstEII hphi bsgI

bspMI

hqiAI/aspHI

ec1136II **bsp1286 bsinkai** 

hindIII csp6I aluI

CCATATCCAC GAIGCATAAA IGIGACCATA GIIGICIIIG GICCIIIICG AGCTIIGAI GACTAAAIGI IICATAGGII AGCTAAGAGA CCICAGGGAA 601 GGTATAGGTG CTACGTATTT ACACTGGTAT CAACAGAAAC CAGGAAAAGC TCCGAAACTA CTGATTTACA AAGTATCCAA TCGATTCTCT GGAGTCCCTT bpmI/gsuI[dcm-] **DSmFI** claI/bsp106 bspDI[dam-] tfir hinfI × × aluI apyI[dcm+] ecoRII bstNI SCIFI dsaV mvaI barI

hinfi

plei

scal plaili 701 CTCGCTTCTC TGGATCCGGT TCTGGGACGG ATTICACTCT GACCATCAGC AGTCTGCAGC CAGAAGACTT CGCAACTTAT TACTGTTCAC AGAGTACTCA csp6I G V rsaI R F S LIYK mbolI bpuAI ppsI fnu4HI bsoFI bbvI P K scfI pstI bsdI ک ک O O K H H alwI[dam-] bsmFI mbol/ndeIl[dam-] dpnII[dam-] bstYI/xhoII dpnI[dam+] alwI[dam-] hpaII TYL ball Idem bsaWI sau3AI nlaIV DamHI 32 G I G A

GAGCGAAGAG ACCTAGGCCA AGACCCTGCC TAAAGTGAGA CTGGTAGTCG TCAGACGTCG GTCTTCTGAA GCGTTGAATA ATGACAAGTG TCTCATGAGT

S

Y C S

ATX

E D F

SLOP

T I

FT

SGTD

ი ი

R F S

1 TGTCCCGCTC ACGITTGGAC AGGGTACCAA GGTGGAGATC AAACGAACTG TGGCTGCACC ATCTGTCTTC ATCTTCCCGC CATCTGATGA GCAGTTGAAA ACAGGGCGAG IGCAAACCIG ICCCAIGGII CCACCICIAG IIIGCIIGAC ACCGACGIGG IAGACAGAAG IAGAAGGGCG GIAGACIACI CGICAACIII SDE I F P P acil ipoli Ilodm PpuAI ppsI SVF KRTV A P fnu4HI **bsofI** bbvI mbol/ndell[dam-] dpnII[dam-] dpnI[dam+] sau3AI VEI beaJI styI asp718 csp6I acc651 rsal nlaIV hgici kpnI banI T F G O maell bsrBI V P L acil bamFI

#### FIG. 41C

maeIII apyI[dcm+] bstNI bsaJI 901 TCTGGAACTG CTTCTGTTGT GTGCCTGCTG AATAACTTCT ATCCCAGAGA GGCCAAAGTA CAGTGGAAGG TGGATAACGC CCTCCAATCG GGTAACTCCC AGACCTIGAC GAAGACAACA CACGGACGAC TIAITGAAGA TAGGGTCTCT CCGGTTTCAT GTCACCTTCC ACCTATTGCG GGAGGTTAGC CCATTGAGGG GNSO r o s ball mnlI Z Z > X X csp6I rsal haeIII/palI PRE ARV haeI mnlI N Fi asp700 XmnI Ω 1 cac8I s v 132 S G T A asp700 X T U M X

ecoRII

dsav

BCLFI

mvaI

fnu4HI bsoFI

cellI/espI

acci cac8i blpI/bpull02I hqaI ddeI Indd Ilnm ddeI scfI

01 AGGAGAGTGT CACAGAGCAG GACAGCAAGG ACAGCACCTA CAGCCTCAGC AGCACCCTGA CGCTGAGCAA AGCAGACTAC GAGAAACACA AAGTCTACGC TCCICTCACA GIGICICGIC CIGICGIICC IGICGIGGAI GICGGAGICG ICGIGGGACI GCGACICGII ICGICIGAIG CICIIIGIGI IICAGAIGCG VYA EKHK A D Y L S K STLT SIS T ഗ SKD ۵ maelll

hgiAI/aspHI ec1136II **bsp1286 bs1HKAI** cac8I hqijii aluI haeIII/palI Bau96I banII BStI BacI bmyI asul ddel

bfaI mael I mu sau96I hgaI mbol/ndeII[dam-] mnlI sau3AI

haeIII/palI asuI hpall sfaNI dpnII[dam-] mspI aluI dpnI[dam+] tru9I

alwI[dam-]

msel

CIGCGAAGIC ACCCAICAGG GCCIGAGCIC GCCCGICACA AAGAGCIICA ACAGGGGAGA GIGTIAAGCI GAICCICIAC GCCGGACGCA ICGIGGCCCI GACGCTTCAG TGGGTAGTCC CGGACTCGAG CGGCCAGTGT TTCTCGAAGT TGTCCCTCT CACAATTCGA CTAGGAGATG CGGCCTGCGT AGCACCGGGA  $\mathbf{c}$   $\mathbf{c$ alwNI[dcm-] maelil

aluI

maelll

ecool091/drall

#### FIG. 41[

```
1301 CTACAAACGC GTACGCTGAG GTTCAGCTAG TGCAGTCTGG CGGTGGCCTG GTGCAGCCAG GGGGCTCACT CCGTTTGTCC TGTGCAGCTT CTGGCTACTC
                                                                                                                                                                                                                                                                                                          GATGITIGCG CATGCGACIC CAAGICGAIC ACGICAGACC GCCACCGGAC CACGICGGIC CCCCGAGIGA GGCAAACAGG ACACGICGAA GACCGAIGAG
                                                           TCATGCGTTG ATCAGCATTT TTCCCATAGA TCTCCAACTC CACTAAAATA CTTTTCTTA TAGCGTAAAG AAGAACGTAG ATACAAGCAA AAAAGATAAC
                                           1201 AGIÀCGCAAC TAGTCGTAAA AAGGGTATCT AGAGGTTGAG GTGATTTTAT GAAAAAGAAT ATCGCATTTC TTCTTGCATC TATGTTCGTT TTTTCTATTG
                                                                                                                                                                                                                                     alwNI[dcm-]
                                                                                                                                                                                                                                                    fnu4HI
                                                                                                                                                                                                                                                                 bsoFI
                                                                                                                                                                                                                                                                                  bbvI
                                                                                                                                                                                                                       aluI
                                                                               L A S
                                   mboll sfaNI
                                                                                IAFL
                                                                                                                                                                                                                                       bsp1286
                                                                                                                                                                                                                                                                                      banll
                                                                                                                                                                                                                                                     apyI[dcm+] bsaJI bmyI
                                                                                                                                                                                                                                                                    haeIII/pall apy1[dcm+]
                                                                                                                                                                                                                         dsav bstNI hgiJII
                                                                                                                                              ecoRII
                                                                                                                                                                                                                                                                                                                                 V Q P G
                                                                                                                 scrFI
                                                                                                                                                              dsaV
                                                                                                                                mvaI
                                                                                  K
N
                                                                                                                                                                                            fnu4HI
                                                                                                                                                                                                                                        bstNI bsoFI
                                                                                                                                                                                                                                                                                       bbvI
                                                                                                                                                                                                           ecoRII
                                                                                                                                                                              SCLFI
                                                                                                                                                                                               mvaI
                                                                                                                                                                                                                                                                                                                                     n
B
                                                                                                                                                                                                                                                                                        acil hael
                                                                                                                                                                                                                                                                                                                                       G
                            hphI
                                        xbal mull mull
                                                                                                                                                                                                                                                                                                                                      0 s 0
                            bfaI
             mael
rmal
                                                                                                                                                                                                                                                                                                                                       VOLV
                                                                                                                                                                                                                                                                             bfaI
                                                                                                                                                                                                                                                rmaI
                                                                                                                                                                                                                                                               mael
                                                                                                                                                                                                                                                                              mluI csp6I mnlI
                                                                                                                                                                                                                                                                                                                                           YAE
                                                                                                                                                                                                    DsiWI/splI
                                                                                                                                                                                                                                  fnuDII/mvnI
                                                                                                                                                                                                                                                                bsh1236I
                                                                                                                                                                                     rsaI
                mael
                                bfaI
    rmaI
                                                                                                                                                                                                                                                    batuI
                                                                                                                                                                                                                                                                                                                                             T
N
                                  rsaI
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ecoRII scrFI mvaI xmaI/pspAI hpaII cauli mspI dsaV caull ball SCIFI ncil dsaV bslI ncil smaI

SCIFI

FIG. 41E

maeII bsaAI TACGTATAAT T Y N T Y N CGCCAGATAA A V Y Y Sau96I haeIII/palI sau96I nlaIV hgiJII bspl286 bspl20I	banII asuI co01091/draII GGGCC CCCGGG G P
VNI NI Sau3AI I[dcm+]  mbol/ndeII[dam-]  dpnI[dam-]  pnI[dam-]  maeII  AGATATATT GATCCTTCCA ATGGTGAAAC TACGTATAAT  ACCTTACCA ACCTATATAA CTAGGAAGGT TACCACTTTG ATGCTAATAAT  ACCTTACCCA ACCTATATAA CTAGGAAGGT TACCACTTTG ATGCTAATAAT  ACCTTACCA ACCTATATAA CTAGGAAGGT TACCACTTTG ATGCTAATAAT  ACCTTACCA ACCTATATAA CTAGGAAGGT TACCACTTTG ATGCTAATAAT  ACCTTACCA ACCTATATAA CTAGGAAACA TACCATATAAT  B W V G Y I D P S N G E T T N N  CACATACCTG CACATGAACA GCCTGCTGC TAGGAATAATA  A Y L Q M N S L R A E D T A V Y Y  A Y L Q M N S L R A E D T A V Y Y  A Y L Q M N S L R A E D T A V Y Y  A Y L Q M N S L R A E D T A V Y Y  A Y L Q M N S L R A E D T A V Y Y  A Y L Q M N S L R A E D T A V Y Y  A Y L Q M N S L R A E D T A V Y Y  A Y L Q M N S L R A E D T A V Y Y  A Y L Q M N S L R A E D T A V Y Y  BABU96  BABU101  BABU1021  BABU103  BABU103  BABU103  BABU103  BABU103  BABU103  BABU103  BABU103  BABU104  BABU104  BABU105  BABU105  BABU105  BABU106  BABU106  BABU107  BABU1	I asul asul apaI apaI apaI apaI apaI styl asul baaJI baaJI baaJI bacCCTCCA CCAAGGCCC AGCCGCAGGT GGTTCCGGG S A S T K G P 125chim2.fab2 ^
bsli sau3AI mbol/ndeII[dam-] dpnI[dam-] alwI[dam-] hphI ATAIT GATCCTTCCA ATGGTGAAAC TATAA CTAGGAAGGT TACCACTTTG I D P S N G E T Cac8I mnlI Cac8I ddeI drdI GAACA GCCTGCGTGC TGAGGACACT CTGT CGACGCACG ACTCCTGTGA N S L R A E D T maeIII bstEII	mval mnll asu ecoRII bsaJI asu dsaV bseRI apa bstNI esp3I mnll bs aIV apyI[dcm+] bsmAI haeIII/pal GAACCTGGT CACGTCTCC TCGGCCTCCA C CTTGGACCA GTGGCAGGG AGCCGAGGT G T L V T V S S A S T seq right is from p6G425chim2.fab2
+) mbol/n  II dpnII[ I TGGGT TGGATATAT  ACCCA ACCTATATAA  W V G Y I  SCfI pstI bspMI ACCTG CAGATGAACA  ACGTG CAGATGAACA  TGGAC GTCTACTTGT  L Q M N S  mae mae bstl	mval mval mval ecoRII bsaJI ecoRII bsaJI bstNI espJI bsaJI hphI bsmBI bsaJI hphI bsmBI apyI(dcm+1 bsmAI crtc crtcGcACCTCTC crtc crtcGcACCA GTGCCACAGG T L V T V S seq right is from p6
dsav bstni bsli sau96i ali asul ecool091/drali draII haelII/pali GGTAAGGGCC TGGATGGG CCATTCCCG ACCTTACCG G K G L E W V G K G L E W V CCAAAAACAC AGCATACCT GGTTTTGTG TCGTATGGA	maell hinll/acyl ahall/bsaHl ql aatll GACGTC TGGGTC GTGCAG ACCCCAG D V W G Q
Pich   Pasa/I   BatM	maeII maeII ecoRII bsaJI asuI hinlI/acyI dsay bseRI apaI ahaII/bsaHI bstNI esp3I apaII bsaJI apuI  ACTGTGCAAG AGGGGATTAT CGCTACAATG GTGACTGGTT CTTCGACGTCAAG GAACCCTGGT CACCGTCTC TCGCCTCCA CCAAGGGCCC TGACACGTTC TCCCCTAATA GCGATGTTAC CACTGACCAA GAAGCTGCAG ACCCCAGTTC CTTGGGACA GTGGCAGAG AGCCGGAGGT GGTTCCCGG  C A R G D Y R Y N G D W F F D V W G Q G T L V T V S S A S T K G P seq right is from p6G425chim2.fab2 ^
sau96I avaII asuI nlaIV bsrI c ACTGGGTCG G TGACCCAGGC H W V R T CACTTTATCT A GTGAAATAGA	hi tr cgctacaatg tr gcgatgttac rr yr g
pleI hinfI taqI xhoI paeR7I avaI maeIII bs: CTCGAGT CACTATATGC ACGAGTCA GTGATATACG TG S S H Y M H I sau96I asu1 AAGTTCA AGGCCGCTT CATTATCAAGT TCCCGGCAAA GT K F K G R F T	mnli NG AGGGATTA TTC TCCCCTAAT R G D Y
ple hin taqI xhoI paeR7I avaI m 401 CTTCTCGG GAAGAGCTC 29 F S S 501 CAAAAGTTC GTTTTCAAG	1 ACTGTGCA TGACACGT 6 C A

#### FIG. 41F

hphI mspI hpaII cfr101/bsrFI bsaWI tth1111/aspI bslI ageI maeIII TCCCGAACC GGTGACGGTG AGGGCTTGG CCACTGCCAC
Parche
nlalv hgiCI banI scrFI mvaI ecoRII hglAI/aspHI dsav hglAI/aspHI dsav beRII bsp1286 bpuAI apyI[dcm+] mnlI bsiHKAI bbsI bsaJI mnlI bmyI mnlI ATCGCTCTC CCCTGGCAC CCTCCTCTTAGCAAG GGGACCGTG GGAGGAGGTT CCGTGGAA S V F P L A P S S K S T S

SCIFI

mvaI

hinpI hhal/cfol hhal/cfol hhal/cfol hhal/cfol hal/cfol hal/cfol hal/cfol hal/spl286 kasi  hinli/acyl cac81 hinli/acyl cac81 hinli/acyl cac81 hinli/acyl cac81 hinli hali
ddeI mblI eco81 I bsu36 CAGTCC TC GTCAGG AG
sef GT CCTA CA GGAT
mspI hpalI scrFI ncil dsaV caulI TCCCGGCT
hinpi hhai/cfoi hhai/cfoi nlaiv hail hail hinli/acyi hgiCi haeli haeli bani cac8i hpai) hgiCi haeli baofi bani acii apali/snoi dsav ddel ahail/baaHi nspBii alw441/snoi cac8i hpai) hpai) haeli baofi acii acii acii acii acic cacGcCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
cace fuu4HI bsoFI i acil i acil i ACCAGGGC (
hinpI hhal/cfoI nlaIV narI kasI hinlI/acyI fnu4HI hgiCI bsoFI banI cr CAGGGGCCCT GACCAGGGG GA GTCGGGGGA CTGGTGGCG S G A L T S G
dd TCGTGGAACT AGCACCTTGA S W N S

CCAGCAGCTT GGGCACCCAG ACCTACATCT GCAACGTGAA TCACAAGCCC AGCAACACCA AGGTGGACAA GAAAGTTGAG CCCAAATCTT GTGACAAAAC GGTCGTCGAA CCCGTGGGTG TGGATGTAGA CGTTGCACTT AGTGTTGGG TCGTTGTGGT TCCAGCTGTT CTTTCAACTC GGGTTAGAA CACTGTTTG S S L G T Q T Y I C N V N H K P S N T K V D K K V E P K S C D K T

maeIII

bsp1286 hgiJII

taqi sall

styl hincll/hindll bmyl bsayl acci banll

bsaJI accI

hinfI tfiI

**bsp1286** 

bmyI

hgici nlaIV

aluI fnu4BI baofi bbvI bstXI

banI

maell

bfaI rmaI mael 2001 TCACACATGC CCGCCGTGCC CAGCACCAGA ACTGCTGGC GGCCGCATGA AACAGCTAGA GGACAAGGTC GAAGAGCTAC TCTCCAAGAA CTACCACCTA AGTGTGTACG GGCGGCACGG GTCGTGGTCTT GATGGTGGAT TTGTCGATCT CCTGTTCCAG CTTCTCGATG AGAGGTTCTT GATGGTGGAT YH S earI/ksp632I O L E D K V E E L L taqI aluI Iloqu sapI tth1111/aspI aluI mnlI bfaI rmaI maeI eagl/xmaIII/eclXI hacIII/palI nlaIII PPCPAPELLGGRMK function between antibody and leucine zipper acil acil bsoFI bsiEI fnu4HI mcrI eaeI cfrI notI bsp1286 nspHI acil bmyl nlaliI Idsu

fnu4HI

bsoFI

ddeI nlaili mael hpail hpail hswFi scrFi celli/espi rmal hinPI celli/espi mael hswFi cauli hhai/cfoi sau96i plei fnu4Hi acii haeli/pali asuI hinfi bsoFi cagacccrc cararcarac ccrccaga rcrcaggar rcrcaggar rccagac crrtrifatr cagacccrc cararacara cccaca rccagar rccagaccca cararaa	
rmal maeI bfal bsmFI sau96I pleI haeIII/palI asuI hinfI cGGCCCT AGAGTCCCTA 60)	
sphI ddeI nlaIII celII/espI blpI/bpul102I hinPI nspI hhaI/cfoI haeII nspHI hael eco47III cac8I asul GTCGGGGAGC GCTAACCATG CGACGCC CAGCCCTCG CGATTCGTAC GCTGCCGC	
H	
pleI aluI hinfI hindII 2101 GAGAATGAAG TGGCAAGACT CAAAAAGCTT CTCTTACTTC ACCGTTCTGA GTTTTTCGAA	

2201 GITAACICAT GITIGACAGC ITAICAICGA TAAGCITIAA IGCGGIAGII TAICACAGII AAAITGCIAA CGCAGICAGG CACCGIGIAI GAAAICIAAC CAATIGAGTA CAAACIGICG AATAGIAGCI AIICGAAAII ACGCCAICAA AIAGIGICAA IITAAAGAAIT GCGICAGICC GIGGCACAIA CIITAGAIIG nlaIV hqici banI tru9I msel bspDI[dam-] msel acil clal/bsp106 tru91 taqI hindIII aluI hincII/hindII hpaI nlaIII tru9I mseI

ea	fnu4HI bsoFI haeIII/palI aeI frI GG
scrFI mval mval ecoRII dsav hinpI bsaJI hphl apyl[dcm+] hinpI bsaJI fok! scf! http://doi.org/101/001/001/001/001/001/001/001/001/00	occentration of the contraction
ecoRV acil rGCGGGAT A	spHI ac mcrI bsiEI TGTCCG ACG
FI II V bsli Sul acccr CTTGC	hgial/aspHI bsp1286 bsiHKAI bmyI GGA GCACTGTC
haelli, sau961 scrFI ncil al mspl mnli csp61 hpall mspl dsav bslI hpall caull cfr101/bsrFl asul GCCGGTAC TGCCGGCCT	I CGTTCTCC GGTACTCC
sau ncil I mspl csp6i msp1 hpaII fr101/bs3	hinPI hhal/cfoI mstI bslI aviII/fspI rGGGACC C
rsal ms hp cf) cT ATGC	h h ms av TC TATG
GGCTTGG	sfani G ATGCAATT
AGGCAT P	sfa SCGTTG A
sfani I II [dcm+] oki scfi GATG CTGT	hinPI  I I I I I I I I AeII I I I I I I I I
sfani scrFi mvai ecoRii dsav nlaIV bstNi hgiCi bsaJi '' hphi apyi[dcm+] bani maeIII foki scfi cGCACCGTC ACCTGGATG CTGT	hinPI hhal/cf rmal mael nhel fnu4HI haelI bsoFI eco47III bbvI bfaI I cac8I GC TGCTAGCGCT A
V I hphI maeII CCGTC A	fnu4) bsoF bbvI cac81 GCGTGC T
nlaIV mnli hgiCI bsaJI I banI CCT CGGCAC	II C TATGG
mnll bsaJ] fokl GTCATCCT (	maelil børi sccagtcac
hinPI hhal/cfol GCGCTCA TCC	hinPI hhal/c rmaI maeI maeI pheI flu4HI haeII bsoFI eco47II bsvI cac8I cac8I ccGACAGCAT CGCCACTCAC TATGGCGTC TGCTAGGCGT GGCTGTCGTA GCGTCAGGA
hinPI hhal/ hargcgcr tracgcga	1 CCGAC!
0	

CCGCCCCCA GICCIGCICG CITCGCIACT IGGACCACT AICGACIACG CGAICAIGG GACCACACC GICCIGIGGA ICCICIACGC CGGACGCAIC GCCGCCGCGT CAGGACGAGC GAAGCGAIGA ACCICGGIGA IAGCIGAIGC GCIAGIACCG CIGGIGIGG CAGGACACCI AGGAGAIGCG GCCIGCGIAG hpall sfani Idsm dphl[[dam-] alwI[dam-] bstYI/xhoII alwI[dam-] bamHI nlaIV bslI mbol/ndeII[dam-] dpnII[dam-] dpnI[dam+] bstUI nlaIII fuuDII/mvnI bsh1236I taqI nlaIV cac8I acil bsrI fnu4HI bsoFI acil

mbol/ndeIl[dam-]

sau3AI

moli

sau3AI

dpnI[dam+]

#### FIG. 41I

									_	ngivii naeli	bsp1286 eco4/111	DMYL DSPHI NAAL/CLOL	banli nlalil	AAGCCC GAGTACTCGC
					IIIigh	bsp1286	Iwmd	banII	sau3AI cac8I	mpol/udell[dam-]	dpnI[dam+]		mbolI[dam-]	C GATGGGGAAG ATCGGGCTCG CCAC G CTACCCCTTC TAGCCCGAGC GGTG
			hinPI	hhaI/cfoI	nlaIV	narI	kasI	hinl1/acy1	hgiCI	haeII	banI	ahaII/bsaHI	acii cac8i hphi	501 GIGGCCGGCA ICACCGGCGC CACAGGIGCG GIIGCIGGCG CCIATAICGC CGACAICACC GAIGGGGAAG AICGGCIG CLACIICGG CIAIGAGCC Caccggccgi agiggccgcg gigiccacgc caacgaccgc ggataiagcg gcigiagigg ciaccctic iagcccgagc ggigaagccc gagiacicgc
hinPi	hhaI/cfoI	nlaIV	narī	kasi	hinl1/acy1	mapI hqiCI	u	E	I/bsrF	cac8I sqrAI	$\overline{}$	eael hphi ahall/bsaHl	cfrl sfaNl cfr101/bsrFI	501 GTGGCCGGCA TCACCGGCGC CACAGGT CACCGGCCGT AGTGGCCGCG GTGTCCA

haeIII/palI 1 CTTGTTTCGG CGTGGGTATG GTGGCAGGCC CCGTGGCCGG GGGACTGTTG GGCGCCATCT CCTTGCACGC ACCATTCCTT GCGGCGGCGG TGCTCAACGG GAACAAAGCC GCACCCATAC CACCGTCCGG GGCACCGGCC CCCTGACAAC CCGCGGTAGA GGAACGTGCG TGGTAAGGAA CGCCGCCCCC ACGAGTTGCC bsofi hgiAI/aspHI **bsp1286 DSIBKAI** bmyI bslI acil acil fnu4HI acil fnu4HI bsoFI cac8I ahaII/bsallI hhal/cfol hinlI/acyI hinPI nlaIV hgici haeII banI kasī narI **DSmFI** sau961 haeIII/pall caull hpaII asul bsaJI bsaJI SCLFI dsaV ncil Idem eco01091/drall eael cac81 bslI cfrI haeIII/palI dsaI ball nlaIV

hpall CCTCAACCTA CTACTGGGCT GCTTCCTAAT GCAGGAGTCG CATAAGGGAG AGCGTCGTCC GATGCCCTTG AGAGCCTTCA ACCCAGTCAG CTCCTTCCGG GGAGTIGGAT GAIGACCCGA CGAAGGAITA CGICCICAGC GIAITCCCIC ICGCAGCAGG CIACGGGAAC ICTCGGAAGI IGGGICAGIC GAGGAAGGCC Idem bsaWI bsrI aluI bslI sfaNI hqaI hinfI pleI ecoNI ball fnu4HI bsoFI bsrI bbvI Iled Ilam

#### FIG. 41J

```
2901 TGGGCGCGG GCATGACTAT CGTCGCCGCA CTTATGACTG TCTTCTTTAT CATGCAACTC GTAGGACAGG TGCCGGCAGC GCTCTGGGTC ATTTTCGGCG
                                                                                              ACCCGCGCCC CGTACTGATA GCAGCGCGT GAATACTGAC AGAAGAAATA GTACGTTGAG CATCCTGTCC ACGGCCGTCG CGAGACCCAG TAAAAGCCGC
                                                                                                                                                                                                                                3001 AGGACCGCTT TCGCTGGAĞC GCGACGATGA TCGGCCTĞTC GCTTGCGGTA TTCGGAATCT TGCACGCCCT CGCTCAAGGC TTCGTCACTG GTCCGGCAC
                                                                                                                                                                                                                                               TCCTGGCGAA AGCGACCTCG CGCTGCTACT AGCCGGACAG CGAACGCCAT AAGCCTTAGA ACGTGCGGGA GCGAGTTCGG AAGCAGTGAC CAGGGCGGTG
                                                                                                                                                                                  sau96I
                                                                                                                                                                                                    nlaiv
                                                                                                                                                                                                                  avall
                                                     cac8I eco47III
            mspI hinpI
                                        cfr101/bsrFI
                            haeir
fou4HI
                                                                         DSOFI
                            naeI
                                                                     nlaIV
                                                                                                                                                                                                                               tfir
                                                                                                                                                                                                                                                                                                                     eagI/xmaIII/eclXI
                                                                                                                                                                                                                            acil
                                                  Ilodm '
                                                                       IVndq
                                                                                                                                                                                                   mbol/ndell[dam-]
                                                                                                                                                                        haeIII/palI
                                                                                                                                                                                                                           bpmI/gsul[dcm-] dpnII[dam-]
                                                                                                                                                                                                                   dpn1[dam+]
                                                                                                                                                                                bsh1236I sau3AI
                                                                 fnu4HI
                                                                                                                                                    fnuDII/mvaI
                                                                                                                                                                                                               hhaI/cfoI
                                                                                                                                                                     bstul
                                                                                                                                                                                               hinpI
                           bstUI nlaIII
          fnuDII/mvnI
                                                            bcgI
                                         bsh1236I
                                                                       hhaI/cfoI
                                                       hinpi
                                                                                                                                                                               acti
                                                                                                                                                                                            I96nes
                                                                                                                                                                                                            avaII
                                                                                                                                                                                                                          asuI
```

GTTIGCAANG CCGCTCTICG ICCGGTAATA GCGGCCGINC CGCCGGCTGC GCGACCCGAI GCAGAACGAC CGCAAGCGCT GCGCTCCGAC CTACCGGAAG 101 CAÀACGITIC GGCGAGAAGC AGGCCAITAI CGCCGGCAIG GCGCCGACG CGCTGGGCIA CGICTIGCIG GCGIICGCGA CGCGAGGCIG GAIGGCCIIC FIG. 41K

bsh1236I fokI haeIII/palI

thal fnuDII/mvnI

thaI

hgaI

fnuDII/mvnI hhaI/cfoI

thaI

bsiEI fnu4HI

hinpI

eael

cfrI

bsh1236I

acil hgal

cac8I

cac8I

psp14061

maell

bsoFI

cfr101/bsrFI

haeIII/pall hpaII

batuI

fnuDII/mvnI bstur bstur

alwI[dam-] .G .C	II
[ a] FTCAAG	nlalII GGCATG CCGTAC
bsmFI aluI GGGA CAGCT	G GGTT
bsm) TCAGGG	aspHI 6 1. nlaIII CATGGAAC
GA CCA	hgiAI/aspHI bsp1286 bsiHKAI bmyI c8I nlaII GAGC ACATGG
GATGAC	I hgiA: bspl: bsiHl bmyI cac8I cGGCGAGC
bspMI  I  III  II  GCMG TA  CCGTCC AT	mnll bsaJI acil fnu4HI bsoFI bgll GCCGC CTC
bspMI scrFI mval ecoRII dsaV bstNI apyI[dcm+]	a fn bs bg TTATGC
H CO	dam-]
thaI fnuDII/mvnI bstUI haeI bsh1236I haeIII/pal aciI cac8I nlaIII CCGCGTTGCA GGCCATGCTG	6I sau3AI mbol/ndeII[dam-] dam-] nspBII maeIII dpnI[dam+] cccrcarc GrcAcGcCGA
thai fnuDII/mvnI bstUI haeI I cac8I cil cac8I CGCGTTGCA GG	sau3AI mbol/ndeII "-] HBII maeII dpnI[dam+] CTGATC GTCAC
thai fnuDi bstUI cacBi NI bshl2 acii GC CCGCT	sau96I avaII :I asuI leII[dam- lm+] nspB lam-] rGG ACCGC
ca sfaNI fokI GGATGC	sau96I avali bsrl sau3AI asul ml mbol/ndell[dam-] dpu1[dam-] apt1[dam-] i[dam-] cGATCACTGG ACCGCTG
HI YI msli Mfani SC ATCG	s bsrI sau3AI a mbo1/nde dpnI[dam dpnII[da taq1[dam-] tT CGATCACTG
fnu4HI bsoFI acil mspI mslI hpaII sfaNI ccGGCGCC ATC	CTAACT
m by CG TTC	CC AGG
mboli i TCTTCTC AGAAGAG	I /mvnI 36I nm-]
ml tfii hinfi TGA TT	fnu4HI bsoFI acil thai thai fnuDII/mvnI bstUI '8I bsh1236I leII[dam-] nm+] lam-] rGG GGCTCTT
fnu4HI bsoFI cac tfiI mspI mslI sfaNI hinfI hpaII sfaNI fokI GGGTATTATGA TTCTTCTCGC TTCCGGCGC ATCGGGATGC GGGTAATACT AAGAAGAGCG AAGGCCGCCG TAGCCCTACG	fnu4HI bsoFI acil thai thai thai thai thai thai thai thai
3201 C	8010

haeIII/pall sau961 sau961 scrFI scrFI thaI thaI ncil mspl fnuDII/mvnI mspl fnuDII/mvnI hpaII bstUI bstUI dsav bsh1236I bsh1236I nlaIV asuI taqI cachII/bsrFI ccrccccc rrccrccc crccrccc ccccccc cccccc
haeIII/pall sau961 scrFI ncil mspI hpaII dsav r asuI mnlI caulI mnlI ccGGGCCACC TCGACCTGAA
haeIII/pall sau961 scrFI thaI thaI ncil fuuDII/mvnI mspI bstUI bstUI dsav bsh1236I bsh1236I nlaIV asuI taqI mnlI acil hgaI acil nlaIII cauII mnlI . CCTCCCCGC TTGCGTGGG GTGCATGGAG CCGGGTGC AGCTG
thai thuDIJ fnuDII/mvni bstUI bstUI bsh12361 bsh12: acil hgal acil CCGCC TTGCGTCGCG
mnli e
fnu4HI bsoFI hinPI hhal/cfoI nlalV narI kasI hinll/acyI hgiCI haeII banI aciI ahaII/bsaHI 1 GATTGTAGGC GCGGGGATA TGGAACAGAC

FIG. 41L

hgaI thaI aciI

hhaI/cfoI

### FIG. 41M

3701 CGGGGTTGCC TTACTGGTTA GCAGAATGAA TCACCGATAC GCGAGCGAAC GTGAAGCGAC TGCTGCTGCA' AAACGTCTGC GACCTGAGCA ACAACATGAA GCCCCAACGG AATGACCAAT CGTCTTACTT AGTGGCTATG CGCTCGCTTG CACTTCGCTG ACGACGACGT TTTGCAGACG CTGGACTCGT TGTTGTACTT

bsh1236I maeII

tfiI hinfI

barI

fuuDII/mvnI

bstuI

cac8I

thaI

ddel

maeII

bsoFI bbvI

GIAGAGGICG ICGGCGIGCG CCGCGIAGAG CCCGICGCAA CCCAGGACCG GIGCCCACGC GIACIAGCAC GAGGACAGCA ACICCIGGGC CGAICCGACC

fnu4HI bsoFI bbvI fnu4HI

```
3801 TGGTCTTCGG TITCCGTGTT TCGTAAAGTC TGGAAACGCG GAAGTCAGCG CCCTGCACCA TIATGTTCCG GATCTGCATC GCAGGATGCT GCTGGCTACC
                                                                                                ACCAGAAGCC AAAGGCACAA AGCATTCAG ACCTTTGCGC CTTCAGTCGC GGGACGTGGT AATACAAGGC CTAGACGTAG CGTCCTACGA CGACGATGG
                                      fnu4HI
                                                       bsoFI
                                                                      bbvI
                             mrol bsaBI[dam-]
                                                               bspEI[dam-]
                 hpall
                                              DSPMII
Idsm
                                                                    hhaI/cfoI
                                                 fnuDII/mvnI hinPI
                                                                 bstur
                   acil
                                   thaI
                                    TIOqu
                                                    DpuAI
                                                                     Isqq
```

mbol/ndell[dam-]

sau3AI

mam[[dam-] dpnI[dam+]

dpnII[dam-]

bstYI/xhoII alwI[dam-]

3901 CTGTGGAACA CCTACATCTG TATTAACGAA GCGCTGGCAT TGACCCTGAG TGATTTTTCT CTGGTCCCGC CGCATCCATA CCGCCAGTTG TTTACCCTCA GACACCTTGT GGATGTAGAC ATAATTGCTT CGCGACCGTA ACTGGGACTC ACTAAAAAGA GACCAGGGCG GCGTAGGTAT GGCGGTCAAC AAATGGGAGT fokī sfani acil acil **DamFI** aan96I nlaIV hhaI/cfoI cac8I hinpr tru91 haell

GTTGCAAGGT CATTGGCCCG TACAAGIAGT AGTCATTGGG CATAGCACTC GTAGGAGAGA GCAAAGTAGC CATAGTAATG GGGGTACTTG TCTTTAAGGG 001 CÂACGITCCA GIAACCGGGC AIGITCAICA TCAGIAACCC GIATCGIGAG CAICCICICI CGITICAICG GIATCAIIAC CCCCAIGAAC AGAAATICCC mnll fokI dsaV nlaIII maelli nspHI BCLFI hpall Caull ncir Idem pall Psp1406I maeII

FIG. 41N

apol ball

cac8I sau96I

haeIII/palI asuI mseI

tru91

GGAATGIGCC ICCGIAGIIC ACIGGIIIGI CCIIIIIIGG CGGGAAIIGI ACCGGGCGAA AIAGICIICG GICIGIAAII GCGAAGACCI CIIIGAGIIG 4101 CCTTACACGG AGCCATCAAG TGACCAAACA GGAAAAAACC GCCCTTAACA TGGCCCGCTT TATCAGAAGC CAGACATTAA CGCTTCTGGA GAAACTCAAC bpmI/gsuI[dcm-] msel acil bsli nlaili acil maelll mnlI

4201 GAGCTGGACG CGGATGAACA GGCAGACATC TGTGAATCGC TTCACGACCA CGCTGATGAG CTTTACCGCA GCTGCCTCGC GCGTTTCGGT GATGACGGTG acil bbvi bsh1236I hphI fouDII/mvoI fnuDII/mvnI hhaI/cfoI mnll bshl236I bstuI hinPI thal bstul thaI fnu4HI **bsoFI** Ilaqsu aluI DVuII fnu4HI bsoFI bcgIbbvI aluI malI asp700 hinfi tfiI XmnI funDII/mvnI **bsh1236I** aluI hgaI fokI bstul acil

CICGACCIGO GCCIACIIGI COGICIGIAG ACACIIAGOG AAGIGCIGGI GOGACIACIO GAAAIGGOGI CGACGGAGOG CGCAAAGOCA CIACIGOCAC

drdI Caull hpall SCIFI Idem foki dsaV ncil sfani acil aluI maeIII esp31 bamBI **DBMAI** hpaII Idem Caull BCLFI nspHI aluI bslI ncil daav fpu4HI **bsoFI** bbvI nlaIII molI

betul acil

fauDII/mvaI

hqaI

thaI

hinPI nspBII

bsh1236I

hhaI/cfoI

FIG. 410

1301 AMANICICIG ACACAIGCAG CICCCGGAGA CGICACAGC TIGICIGIAA GCGGAIGCCG GGAGCAGACA AGCCCGICAG GGCGCGICAG CGGGIGIIGG TITIGGAGAC IGIGIACGIC GAGGGCCTCI GCCAGIGICG AACAGACAII CGCCIACGGC CCICGICIGI ICGGGCAGIC CCGCGCAGIC GCCCACAACC

bsp1286	<b>DSIHKAI</b>	bmyI ndeI	apaLI/snoI		SIW441/BBOL	GAGTGCACC	じじょじしゅしょし	
		ddeI	raal	1	Capet	A GATTGTACTG A	THE CHAPTER CHAPTER	י רועערטירטיר י
	sfani	fnu4HI	heofit	1 1050	acil	FATGCGG CATCAGAGC		ALACGCC GLASTICACS
			+ r.00T	7777	mseI	CIT AACT		SAM LIST
			Lat1107T + T109T	DSCITOLI	acil acci bsri msel	GTGT ATACTEG		CACA TATGACC
					acil	r AGCGGA		A TCCCCI
<b>+</b>	TIORE	TOKE	11 (1) (1)	hinpi nlaiii bsri bsaAi	hhar /ofor +th1111/agnI	DIRECTOR CONTROL OF THE ACTUAL ACCIONATION ACCIONATION AND THE CONTROL OF THE ACTUATION OF THE ACTUAL ACCIONATION OF THE ACTUATION OF THE ACTUAL ACCIONATION OF THE ACCIONATION OF THE ACTUAL ACCIONATION OF THE ACTUAL ACCIONATION OF THE ACTUAL ACCIONATION OF THE ACTUAL ACCIONATION OF THE ACCIO	CA IGACCCAGA ACCAMONA	GCCCACAGCC CCGCGTCGGT ACTGCGTCAG TGCATCGCTA TCGCCTCACA TAGAINCACC GIAGILICGI CIAACAIGAC TCTCACACACACACACACACACACACACACACACACA
foutur	110051	Daor	7 000	hinPI	Phat/C		00000	CCCCCTC
							1 5666161666	GCCCACAGGC

hqiAI/aspHI

401

Iloqm

acii acii bavi baiEI 501 ATATGCGGTG TGAAATACCG CACAGATGCG TAAGGAGAAA ATACCGCATC AGGCGCTCTT CCGCTTCCTC GCTCACTGAC TCGCTGCGCT CGGTCGTTCG TATACGCCAC ACTITATGGC GIGICTACGC ATICCICITI TAIGGCGIAG ICCGCGAGAA GGCGAAGGAG CGAGIGACIG AGGGACGCGA GCCAGCAAGC MCLI hhaI/cfoI hinPI fnu4HI **bsoFI** pleI earI/ksp632I hhaI/cfoI sapI hinPI sfaNI

haeIII/palI bi getecegega ecestateas eteacteaaa gecegtaata egettateea eagaateage ggataacgea ggaaagaaca tetgageaaa aggeeageaa CGACGCCGCT CGCCATAGIC GAGIGAGIII CCGCCAITAI GCCAATAGGI GICITAGICC CCTAIIGCGI CCITICIIGI ACACICGIII ICCGGICGII ball cac8I haeI nlaIII aflIII IBdsu Idsu hinfI acil aluI acil barBI cacel fnu4HI **bsoFI** acil fnu4HI **bsoFI** bbvI

AAGGCCAGGA ACCGTAAAAA GGCCGCGTTG CTGGCGTTTT TCCATAGGCT CCGCCCCCT GACGAGCATC ACAAAAATCG ACGCTCAAGT CAGAGGTGGC TTCCGGTCCT TGGCATTTTT CCGGCGCAAC GACCGCAAAA AGGTATCCGA GGCGGGGGA CTGCTCGTAG TGTTTTAGC TGCGAGTTCA GTCTCCACCG mpli drdI hgaI tagI sfanī acil nlaIV cac8I fnuDII/mvnI haeIII/palI fnu4HI bsoFI acil **bsh1236I** batuI thaI bali apyI[dcm+] hacIII/palI hael nlaIV ecoRII bstNI SCLFI dsaV mvaI

FIG. 41P

			bslI	acil mspl	fnu4HI hpaII	bsoFI bsaWI acil	CGTTTCCCCC TGGAAGCTCC CTCGTGCGCT CTCCTGTTCC GACCCTGCCG CTTACCGGAT ACCTGTCCGC GCAAAGGGGG ACCTTCGAGG GAGCACGCGA GAGGACAAGG CTGGGACGGC GAATGGCCTA TGGACAGGCG	
scrFI	mvaI	ecoRII	dsaV	bstNI hinPI	apy1[dcm+] bssSI	apyI[dcm+] bsaJI aluI mnlI hhaI/cfoI	SCATACCCCC IGGAAGCICC CICGIGCGCI CICCI SCAAAGGGGG ACCIICGAGG GAGCACGCGA GAGGA	
	scrFI	mvaI	ecoRII	dsaV	batni	apy1 [dc	4801 GAMACCGAC AGGACTATAA AGATACCAGG C CTTTGGGCTG TCCTGATATT TCTATGGTCC G	

DSINKAI	bmyI	apaLI/snoI	alw44I/snoI	TGTGCACGAA	ACACGIGCII
			aluI	4901 CITICICCCI ICGGGAAGCG IGGCGCITIC ICAIAGCICA CGCIGIAGGI AICICAGIIC GGIGIAGGIC GIICGCICCA AGCIGGGCIG IGIGCACAA	SANAGAGGA AGCCCTTCGC ACCCCGAAAG AGTATCGAGT GCGACATCCA TAGAGTCAAG CCACATCCAG CAAGCGAGGT TCGACCCGAC ACACGTGCTT
				GIICGCICCA	CAAGCGAGGT
				GGTGTAGGTC	CCACATCCAG
			ddeI	ATCTCAGTTC	TAGAGTCAAG
			scfI	CGCTGTAGGT	GCGACATCCA
		_	aluI	TCATAGCTCA	AGTATCGAGT
	hinPI	hhaI/cfoI	haell	TGGCGCTTTC	ACCCCCAAAG
				TCGGGAAGCG	AGCCCTTCGC
				CTTTCTCCCT	GNAAGAGGGA
				4901	

hgiAI/aspHI

bsp1286

alwn[dcm-]	fnu4HI	bsoFI	fnu4HI	bsoFI	bbvi maelli	hort bhirt hort
	Idsm	hpall	scrFI	ncil	pleI dsav	
			nspBII maeIII	Idsm Idc	bsaWI	at /ofot heatt
	fpu4HI	bsoFI	IIBqen	acii hin	mcrI bbvI	heirt hha

DSTI DDVI DSTI	GCCACTGGTA	CGGTGACCAT	
DOVI	GCAGCA	CCICCI	
DSLI	ACTG	TGAC	
	ACTTATCGCC	TGAATAGCGG	
	GTAAGACACG	CATTCTGTGC	
cauli	CCAACCCG	NGGTTGGGC	
nintl	001 CCCCCCGTTC AGCCCGACCG CTGCGCCTTA TCCGGTAACT ATCGTCTTGA GTCCAACCCG GTAAGACACG ACTTATCGCC ACTGGCAGCA GCCACTGGTA	GGGGGGCAAG ICGGGCIGGC GACGCGGAAI AGGCCAIIGA IAGCAGAACI CAGGIIGGGC CAIICIGIGC IGAAIAGCGG IGACCGICGI CGGIGACCAI	
npall	TCCGGTAACT	AGGCCATTGA	
DSIEI NABI/CIOI NE	CTGCGCCTTA	GACCCCCGAAT	
DSIEI	AGCCCGACCG	TCGGGCTGGC	
	CCCCCCGTTC	GGGGGGCAAG	
	001		

	hinPI	hhaI/cfoI	ATTIG GTATCIGCGC	TAAAC CATAGACGCG
rmaI	maeI	bfaI	GCTA CACTAGAAGG ACAGT	CGAT GTGATCTTCC TGTCA
bsli	haeIII/palI	haeI	G TGGTGGCCTA ACTACG	C ACCACCGGAT TGATGC
		acii scfi	101 ACAGGATTAG CAGAGCGAGG TATGTAGGCG GIGCTACAGA GITCTIGAAG IGGIGGCCIA ACTACGGCTA CACTAGAAGG ACAGTATIG GIAICTGCGC	GICCTAATC GICTCGCTCC ATACATCCGC CACGATGTCT CAAGAACTTC ACCACCGGAT TGATGCCGAT GTGATCTTCC TGTCATAAAC CATAGACGCG
		mnlI	01 ACAGGATTAG CAGAGCGAGG TH	TGTCCTAATC GTCTCGCTCC A;

FIG. 41Q

nlaIII DapHI rcal 5301 ATTACGCCCA GAAAAAAGG ATCTCAAGAA GATCCTTTGA TCTTTTCTAC GGGGTCTGAC GCTCAGTGGA ACGAAAACTC ACGTTAAGGG ATTTTGGTCA TAAIGCGCGT CITITITIC TAGAGIICIT CTAGGAAACT AGAAAAGAIG CCCCAGACTG CGAGICACCT IGCITIIGAG IGCAAIICCC IAAAACCAGI 5201 TCTGCTGAAG CCAGTTACCT TCGGAAAAAG AGTTGGTAGC TCTTGATCCG GCAAACAAC CACCGCTGGT AGCGGTGGTT TTTTTGTTTG CAAGCAGCAG AGACGACTIC GGICAAIGGA AGCCIITIIC ICAACCAICG AGAACIAGGC CGIITGIIIG GIGGCGACCA ICGCCACCAA AAAAACAAAC GIICGIGGIC fnu4HI **bsoFI** bbvI cacBI tru91 mseI maell acii nspBII acil hgal ddel mboI/ndeII[dam-] dpnII[dam-] alwI[dam-] dpnI[dam+] mbol/ndell[dam-] hpaII Idem sau3AI dpnII[dam-] mboII[dam-] dpnI[dam+] mbol/ndeII[dam-] sau3AI aluI dpnII[dam-] alwI[dam-] dpnI[dam+] alwI[dam-] bstYI/xhoII gau3AI mbol/ndeII[dam-] dpnII[dam-] bstYl/xhoII dpnI[dam+] maeIII eco571 bsrI fuuDII/mvaI hhaI/cfoI **bsh1236I** hinpi bstul thaI

ahaIII/draI tru9I mseI tru9I msel ahaIII/draI mbol/ndeII[dam-] tru9I mseI dpnII[dam-] bstri/xhoII bstri/xhoII alwI[dam-] dpnI[dam+] Bau3AI mbol/ndell[dam-] alwI[dam-] bfaI mael rmaI mpoII[dam-] dpnII[dam-] hphI dpnI[dam+]

5401 TGAGATTATC AAAAAGGATC TTCACCTAGA TCCTTTTAAA TTAAAAATGA AGTTTTAAAT CAATCTAAAG TATATATGAG TAAACTTGGT CTGACAGTTA ACTETAATAG ITITICETAG AAGIGGAICI AGGAAAATIT AAITITIACI TEANAATITA GITAGAITIC ATATATACIC AITIGAACCA GACIGICAAI

ahdI/eam1105I hinfI pleI fokI mbol/ndeII[dam-] dpnII[dam-] dpnI[dam+] sau3AI ddeI nlaIV hqici banI mnlI tru9I mseI

501 CCAATGCTTA ATCAGTGAGG CACCTATCTC AGGGATCTGT CTATTTCGTT CATCCATAGT TGCCTGACTC CCCGTCGTGT AGATAACTAC GATACGGGAG GGTIACGAAT TAGTCACTCC GTGGATAGAG TCGCTAGACA GATAAAGCAA GTAGGTATCA ACGGACTGAG GGGCAGCACA TCTATTGATG CTATGCCTC

FIG. 41R

I haeIII/palI gau96I hinPI asuI hhaI/cfoI A AGGCCGAGC	maell hinpl hhal/cfol mstl psp14061 avill/fsp1 T TGCGCAACGT
mspI hpaII bglI cac8I ; CAATAAACCA GCCAGCGGA	tru9I bsrI mseI G TAGTTCGCCA GTTAATAGT
bpml/gsul[dcm-] mspl hpall cfrl01/bsrFl hphl nlalV TC ACCGCTCCA GATTTATCAG	scrFI ncil mspl hpall rmal dsaV mael caull bfal rTGCGGGAAG CTAGAGTAAC
bsmAI bsaI thaI thaI fnuDII/mvnI bstUI bsh1236I aciI ATACGGGAG ACCCACGCTC TATGGGGGTC TGGGTGCGCAC	scrFi ncil mspi hpali tru91 dsaV I bsrI msel cauli foki asel/asnI/vspI CCATCCAGTC TATTAATIGT TGCCGG
bsal bsal thal thal sau961 fnu4HI fnuDII/mvnI mspl nlaIV bscFI bstUl bstUl bsh12361 hph I nlaIV asuI bbvI acil hph I nlaIV cCGAATGCTA GGGGGTC ACGGGTC ACGGCTCGA GGGCGGAGG GGTCGGCT TCCCGGCTCG CCGAATGCTA GACGGGGTC ATATGGGGGTC TATGGGCGTC TGGGCGCTCGAGGT TGCCGGCTCGAGGT TGCCGGCTC TGGGCGTCGAGGT TGCCGGCTCGAGGT TGCCGGCTCGAGGT TCCCGGCTCGAGGT TGCCGGCTCGAGGT TCCCGGCTCGAGGT TGCCGGCTCGAGGT TATTTTGCT CGGTCGGCTCGAGCTCGAGGT TGCCGGCTCGAGGT TGCCCGGCTCGAGGT TGCCGGCTCGAGGT TGCCGGCTCGAGGT TGCCGGCTCGAGGT TGCCCGCGCTCGAGGT TGCCCGCGCTCGAGGT TGCCCGCGCTCGAGGT TGCCCGCGCTCGAGGT TGCCCGCGCTCGAGGT TGCCCGCGCTCGAGGT TGCCCGCGCTCGAGGT TGCCCGCGCTCGAGGT TGCCCGCCTCGAGGT TGCCCGCCTCGAGGT TGCCCGCCTCGAGGT TGCCCGCCTCGAGGT TCCCGCCTCGAGGT TGCCCCCGCGCTCGAGGT TCCCCCCCCCGCAGGT TCCCCCCCCCC	mael) mael) mapl mspl hpall rmal hpall rmal hhal/cfol avall avall asul noti mspl hpall rmal hpall rmal hhal/cfol caull bfal bfal asul asul cGTCTTCACC AGGACGTTGA GGTAGGTCAG ATAATTAACA ACGGCCTTC GATCTCATTC ATCAATACAT ACGCGTTGCA CGTCTTCACC AGGACGTTGA AATAGGCGGA GGTAGGTCAG ATAATTAACA ACGGCCTTC GATCTCATTC ATCAAGGGGT CAATTATCAA ACGCGTTGCA
501	01

TAFTIED	Thot /rdell [dell-]		gau3AI dpn![dam+]	mpol/ndell[dam-] dpnII[dam-]	ָ ֡ ֡	opurluant unantu	dpnII[dam-] maeIII alwI[dam-]		CANCERTAN GOLDSTING MICHAEL	GTTGCTAGIT CCGCTCAATG TACIAGGGG
			nlaIV	Lost		DSAMI	Iladi Inla	TTTDD	GTTGCCATT GCTGCAGGCA TCGTGGTGTC ACGCTCGTCG TTTGGTATGG CTTCATTCAG CTCCGGTTCC CANCALLAN GGCGAGTTT TTTTTTCCC	CAACGGIAA CGACGICCGI AGCACCACAG IGCGAGCAGC AAACCAIACC GAAGIAAGIC GAGGCCAAGG GIIGCIAGII CCGCICAAIG IACIAGGGG
CACBL	scfI	Dati	foulfit	TURBIT	DSOFT	Tam Thy		DBIDI DBGI BIGHT	GTTGCCATT GCTGCAGGCA TCGTGGTC	CAACGGTAA CGACGTCCGT AGCACCAC

fpu4HI bsoFI bbvI .. nlalli mslI hacIII/palI fnu4HI acil bsoFI eaeI cfrI mbol/ndeII[dam-] mnll dpnII[dam-] dpnI[dam+] sau961 pvuI/bspCI sau3AI asul bsiEI avall mcrl

ATGITGIGCA ANAMAGCGGI TAGCICCTIC GGICCTCCGA ICGITGICAG AAGIAAGTIG GCCGCAGIGI TAICACICAI GGITAIGGCA GCACIGCAIA TACAACACGI IIIIICGCCA AICGAGGAAG CCAGGAGGCI AGCAACAGIC IICAIICAAC CGGCGICACA AIAGIGAGIA CCAAIACCGI CGIGACGIAI

acil alul

#### FIG. 41S

baiEI bcgI mcrI

fuu4HI **bsoFI** acii

rsaI scal bsrI

ddeI maelli hphi csp61 sfani

fokI

TAAGAGAATG ACAGTACGGT AGGCATTCTA CGAAAAGACA CTGACCACTC ATGAGTTGGT TCAGTAAGAC TCTTATCACA TACGCCGCTG GCTCAACGAG 001 ATTCTCTTAC IGTCATGCCA TCCGTAAGAT GCTTTTCTGT GACTGGTGAG TACTCAACCA AGTCATTCTG AGAATAGTGT ATGCGGCGAC CGAGTTGCTC nlaIII

asp700 mboli psp1406I XIUDI hgiAI/aspHI bsp1286 **DSIMKAI** bmyI ahalii/drai tru9I msel fnuDII/mvnI hhaI/cfoI **bsh1236I** hinPI bstuI thaI acil cauli hincii/hindii ahaII/bsaHI hinlI/acyI hqaI hpaII Idem SCLFI ncil dsaV

mbol/ndell[dam-]

sau3AI

dpnII[dam-] bstYI/xhoII

alwI[dam-]

dpnI[dam+]

DI TIGCCCGGCG TCAACACGGG AIAATACCGC GCCACATAGC AGAACTITAA AAGTGCTCAT CATIGGAAAA CGITCTICGG GGCGAAAACT CICAAGGAIC AACGGCCGC AGTIGIGCCC TAITAIGGCG CGGIGIAICG ICIIGAAAII ITCACGAGIA GIAACCIITI GCAAGAAGCC CCGCIITIGA GAGIICCIAG

mbol/ndell[dam-] mpoII[dam-] sfaNI dpnI[dam+] eco57I sau3AI alw44I/snoI hqiAI/aspHI apaLI/snoI **bsp1286 DSIHKAI** bmyI mpol/udell[dam-] tagi dpnII[dam-] dpnI[dam+] alw[[dam-] barI Bau3AI

TIACCGCTGT TGAGATCCAG ITCGATGIAA CCCACTCGTG CACCCAACTG ATCTTCAGCA TCTTTTACTT TCACCAGCGT ITCTGGGTGA GCAAAAACAG AAIGGCGACA ACICIAGGIC AAGCIACAII GGGIGAGCAC GIGGGIIGAC IAGAAGICGI AGAAAAIGAA AGIGGICGCA AAGACCCACI CGIIIIIGIC bstXI/xhoII

dpnII[dam-]

bassI

maelii

IIgdsu

hphI

hphI

earI/ksp632I mslI Enu4HI acii **bsoFI** 

GAAGGCAAAA IGCCGCAAAA AAGGGAAIAA GGGCGACACG GAAAIGIIGA AIACICAIAC ICTICCITIT ICAAIAIIAI IGAAGCAIII AICAGGGIIA CTICCGITII ACGGCGIIII IICCCIIAII CCCGCIGIGC CIITACAACI IAIGAGIAIG AGAAGGAAAA AGIIAIAAIA ACIICGIAAA IAGICCCAAI

SapI

I I oqu

FIG. 411

6401 TTGTCTCATG AGCGGATACA TATTTGAATG TATTTTAGAAA AATAAACAAA TAGGGGTTCC GCGCACATTT CCCCGAAAAG TGCCACGTGA CGTCTAAGAA AACAGAGTAC TCGCCTATGT ATAAACTTAC ATAAATCTTT TTATTTGTTT ATCCCCAAGG CGCGTGTAAA GGGGCTTTTC ACGGTGGACT GCAGATTCTT AACAGAGTAC TCGCCTATGT AACAGAGTAC TCGCCTATGT ATAAACTTAC ATAAATCTTT TTATTTGTTT ATCCCCAAGG CGCGTGTAAA GGGGCTTTTC ACGGTGGACT GCAGATTCTT ahaII/bsaHI aatii ddei hinl1/acy1 maell 6501 ACCATTATTA TCATGACATT AACCTATAAA AATAGGCGTA TCACGAGGCC CTTTCGTCTT CAA  $(S \in \mathcal{U} \cup \mathcal{NO} \cup \mathcal{O})$  TGGTAATAAT AGTACTGTAA TTGGATATTT TTATCCGCAT AGTGCTCCGG GAAAGCAGAA GTT plaiv hhai/cfoi fnuDII/mvnI **bsh1236I** bstul acil Iloqm bpuAI Isqq eco01091/draII haeIII/palI sau96I asaI mnlI tru9I nlaIII bapHI bspHI acil rcal bsmAI bsrBI nlaIII rcal

hinPI

thaI

FIG. 410

>length: 6563

```
1119 1195 1425 1434 1446 1512 1695 1696 1752 2155 2375 2727 3002 3090 3339 3463
                                                                                                                                                           3436 3448 3490 3544 3597 3613 3619 3700 3838 3967 3970 3981 4139 4155 4210 4266
                                                                                                                                                                                                                                                                                                                                                                                                                                                     2218 2233 2889 3292 4202 4259 4270 4319 4338 4619 4845 4935 4981 5238 5759 5859
                                                                                                                             2628 2781 2784 2787 2906 2926 3005 3045 3094 3141 3226 3241 3309 3342 3367 3412
                                                                                                                                                                                      4351 4390 4400 4442 4467 4505 4518 4544 4561 4604 4611 4632 4723 4751 4878 4897
                                                                                                                                                                                                                                                                                                                                                                                                                           72 121 252 320 398 532 589 648 1126 1144 1167 1325 1386 1906 2054 2075 2126
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          412 413 712 713 1171 1471 2578 2579 3300 3870 5245 5319 5331 5416 5429 5893
                                                                                                   178 542 805 877 1340 1750 1826 2011 2039 2043 2182 2242 2384 2492 2501 2504
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       640 999 1347 1357 1449 1665 1713 1755 1764 2333 3262 3645 4705 4826 4839
                                                                                                                                                                                                                  5018 5128 5263 5272 5634 5725 5916 5962 6083 6127 6204 6313 6412 6459
                                                                                                                                                                                                                                                                                                                                           1645 1813 2616 2637 2751 3408 6107 6489
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      1831 4494 4992 6238
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     1831 4494 4992 6238
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 905 930 4234 6166
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            alwNI[dcm-](CAGNNNCTG): 1117 1385 5089
                                                                                                                                                                                                                                                                                                                                                                           5435 5454 6146
                                                       1093 1963 4449
                                                                                                                                                                                                                                                                                                                                                                                                       ahdI/eam11051(GACNNNNNGTC): 346 5566
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        see tthlllI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   1 391 4093
                                                                                   3867[dam-]
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            see hglAI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  6196 6214
                                                                                                                                                                                                                                                            see hinlI
                                                                                                                                                                                                                                                                                          1307 4678
1645 6489
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           see aseI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  403 823
                           403 823
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            1695
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             5742
                                                                                                                                                                                                                                                                                                                        1788
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 5922
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               aseI/asnI/vspI(ATTAAT):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          alw44I/snoI(GTGCAC):
                                                                                                                                                                                                                                                                                                                                                                             ahaIII/draI(TTTAAA):
                                                                                                                                                                                                                                                                                                                                                     ahaII/bsaHI(GRCGYC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         apaLI/snoI(GTGCAC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       asp700 (GAANNNTTC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        alwI[dam-](GGATC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               apyI[dcm+](CCWGG):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    asp718(GGTACC):
                               acc651 (GGTACC):
                                                                                       accili(TCCGGA):
                                                                                                                                                                                                                                                                                              aflii(ACRYGT):
 aatII(GACGTC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     apol(RAATTY):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            apaI(GGGCCC):
                                                             acci (GTMKAC):
                                                                                                                                                                                                                                                                                                                            ageI(ACCGGT):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        asuI (GGNCC):
                                                                                                                   acil(CCCC):
                                                                                                                                                                                                                                                                                                                                                                                                                                             aluI(AGCT):
```

FIG. 41V

Stop Template Primer

5' CAT GGT ATA GGT TAA ACT TAT TTA CAC 3' (SEA ID NO: 63) SL.97.2

5' CAT GGT ATA GGT NNS ACT TAT TTA CAC 3' (SEQ TO NO: 64) NNS Randomization Primer SL.97.3

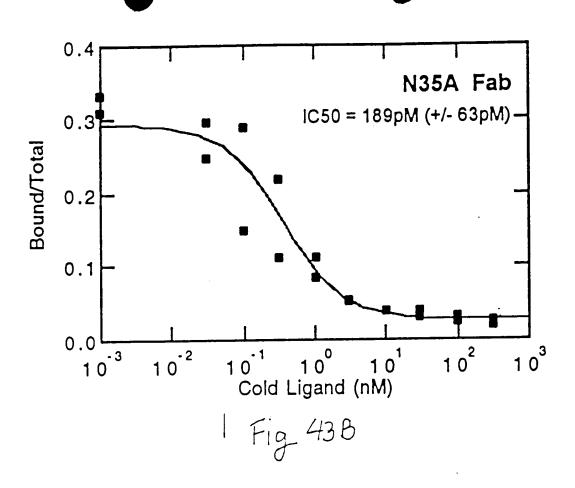
FIG. 42

## Randomization of Position N35 of Variable Light Chain CDR-1 Amino Acid Frequency

Phage Display (NNS Codon Library) Sort #3

Amino Acid	Frequency % Total	% Total	IC50 (nM)
Asparagine (wt)	1	5.6	4.9
Glycine	9	16.6	3.1
Aspartic Acid	3	16.6	3.1
Glutamic Acid	4	22.2	0.1
Alanine	2	5.6	0.2
Lysine		5.6	NO
Serine		1.9	ND

FIG. 43A



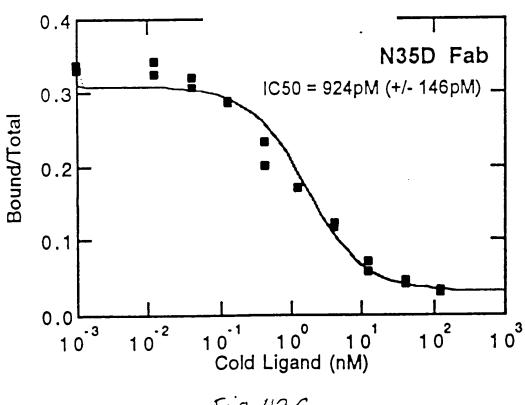
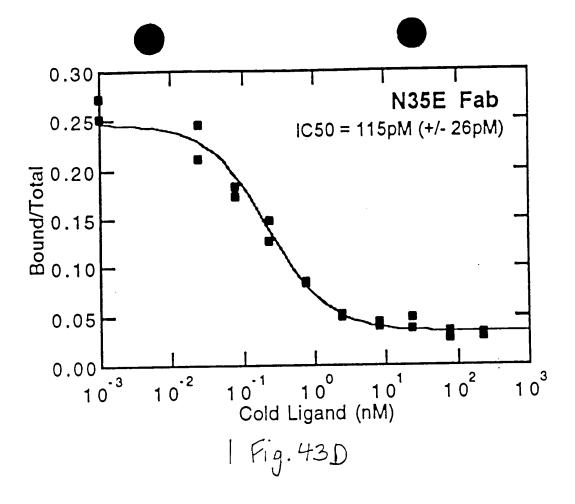
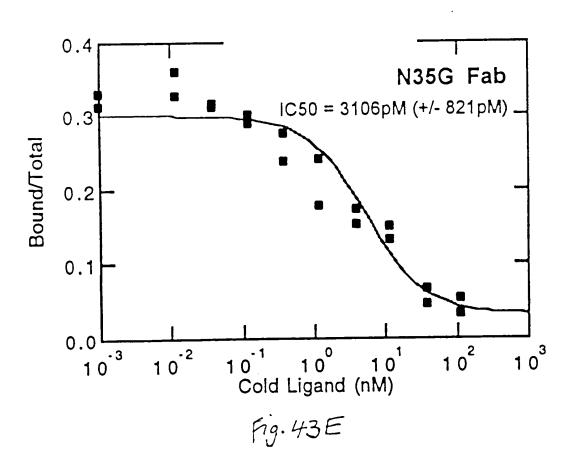
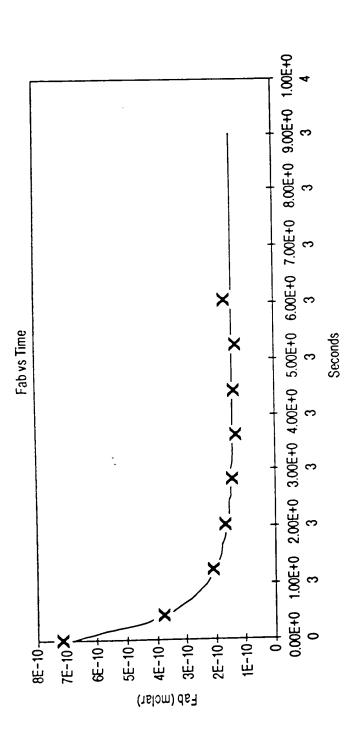


Fig. 43C







Representative Conc versus Time Plot. Shown is the kinetic data for 6G4V11N35A.F(ab')2.

kd Kd	ND 114pM	2.1x10 <sup>-4</sup> 109pM	$^{2} 6 \times 10^{-4}$ 54nM
ka	QN	$2.0 \times 10^6$	$A 7 \times 10^6$
SAMPLE	6G4V11N35A-Fab	6G4V11N35A-F(ab') <sub>2</sub>	CCAVIINISCE Esh

FIG. 44

1	אַ מער ג	ממ	מממ	Δ	אדאדע	GCZ	ATT	TCTT	CT	IGCA	TC	OTA7	TT	CG	TTTT	MC.	TAT	TGC:	rac.	AAAC	
		~~~		m	m 3 m 3 c		מגיד	ACAI	$\alpha \alpha \lambda$	እሮርጥ	AG	ATAC	CAAC	30	AAAA	AAG	AIA	MCG	410	1110	
• •	TACT	. 1.1	111	1	ININ	3 C G .	F. V.V.	TOTA	T.	λ	5	м	F	v	F	S	I	A	T	N	
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	000	· ~	003	^	መእጥአረ		~ጥአ	CTYC	2CT	$c \lambda CC$	ഭവ	TTCC	$\mathbf{G}(G)$	GG	ACAG	بحاياق	JAG	MCM		GCIA	
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	3000	~m~	3.00	Α.	m~ ∧ C(	الكلات	CAG	GTC:	. אמ	ተረ እ አ	AG	TT	AGT.	AC	ATGG	TAT	AGG	TGA	GAC	GTAT	
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301	CIG	ACC	AIC	. A	CCAG	101	CCT	000	TOT.	באנים עג בינים נו	ממ	GCG	 	AA:	TAAT	GAC	:AAG	TGI	CTC	ATGA	
	GAC	TGC	TAC	11	CGTC	AGA	.061	CGG	101	1010	<u>τ</u> .	.GCG	- m	v	v		S	0	S	Т	
78	L	T	I	S	S	L	Q	Þ	E	D	r	А	1	1	Y	_	<u></u>				
361	CAT	GTC	ccc	C	TCAC	GTT	TGG	ACA	GGG	TACC	AA	GGT.	GGA	(GA	TCA	ACC	AAC	TGT	YGG (	CTGCA	
	C T 3	-		~	NOTE:	C 2 2	ACC	TEYP	יררנ	`ATGG	$T^{T}$	'CCA	CCI	CT	AGT	1760	71716	ALF	c	PHCGI	
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	GGT	AG	ACAC	GΑ	AGTA	.GA	4GGG	CGG	TAC	SACTA	. CI	'CG'I	'CAA	AC.T	TTAC	JACC	.116	ACC	, ,,,,,,,	SACAA	
118	P	s	V	F	I	F	P	P	S	D	Ε	Q	L	K	. S	G	T	Α	5	V	
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401	CTY.	·~	-	20	TYCAA	ጥል፤	ירער	СТА	TCC	CAGA	GZ	\GGC	CA	\AG	TAC	AGTO	GAA	GG	NGG A	DAATA	
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	ر ريز	JAC	.GCT	٠,٠	, WOY	บ			T.	S	S	P	v	7	r K	s	F	N	R	G	
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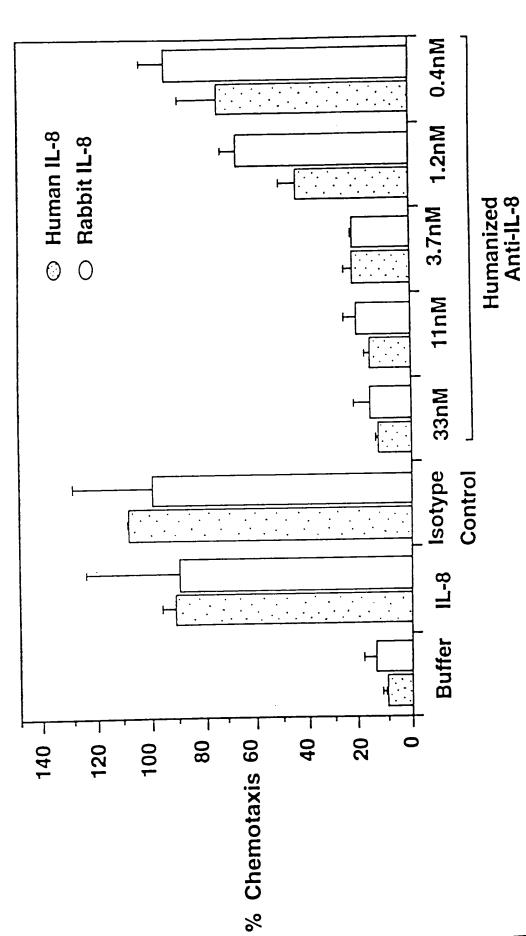


FIG. 46

N35AH1upr

N35AH1lwr

5'-TCGAGAGGAGTAGCCAGAAGCTGCACAGGACAAACGGAGTGAGCCCCCTGGCTGCACCAGGCCACCGCCAGACTGCACT AG-3'

Bold indicates nucleotide change destroying Pvull site.

FIG. 47

>This has the pSVI backbone with the pRK7 cloning linker (pSVI7) and the intron DHFR(ID) >made from pSVI.WTSD.D by adding a linearization linker(LL) into the Hpal site > length: 8120 (cfrcular)

apyI[dcm+] nlaiv ecoRII bstNI SCFFI bsaJI dsav mvaI bsmFI mbol/ndell[dam-] nspBII hinfi tagi[dam-] Iluvq sau3AI aluI pleI dpnII[dam-] dpnI[dam+] pvuI/bspCI tadI[dam-] bsiEI mcrI rmaI mael bfal hgiAI/aspHI ecl136II cac8I **bsp1286 DS1HKAI** hgiJII banII aluI bmyI saci sstI

1 ITCGAGCICG CCCGACATIG ATTATIGACI AGAGICGAIC GACAGCIGIG GAAIGIGIGI CAGITAGGGI GIGGAAAGIC CCCAGGGCICC CCAGCAGGCA AAGCICGAGC GGGICGIAAC IAAIAACIGA ICICAGCIAG CIGICGACAC CITACACACA GICAAICCCA CACCITICAG GGGICCGAGG GGICGICGI

nsiI/avaIII IHdsu cac81 sfaNI ppu10I sphI cac8I apyI[dcm+] bsmFI nlaIV ecoRII bsaJI bstNI dsav mvaľ apyI[dcm+] ecoRII scrFI bstNI dsav mval sexAI nsil/avallI sfani ppu101 nlalii nspHI cac8I Igan sphI

101 GAAGTATGCA AAGCATGCAT CTCAATTAGT CAGCAACCAG GTGTGGAAAG TCCCCAGGCT CCCCAGCAGG CAGAAGTATG CAAAGCATGC ATCTCAATTA CITCATACGI ITCGTACGIA GAGITAATCA GICGIIGGIC CACACCIITC AGGGGICCGA GGGGICGICC GICTICATAC GITTCGIACG TAGAGITAAI

nlalil

styI ncoI

acil acil fokl acil bsrl acil acil bsaJ

201 GTCAGCAACC ATAGTCCCGC CCCTAACTC GCCCTTCCG CCCCTAACTC CGCCCAGTTC CGCCCATTCT CCGCCCCATG GCTGACTAAT TTTTTTATT CAGTCGTTGG TATCAGGCCG GGGTTGAGG CGGGGTTGAG GCGGGGTAAGA GGCGGGGTAC CGACTGATTA AAAAAAATAA bsmFI

#### FIG. 48A

I /eclXI		
haeIII/palI mcrI eagl/xmaIII/eclXI eaeI cfrI baiEI ispl	I & <b>«</b>	TC SA
hae) I mcrI eagl, eael cfrI balE: mspl hpalI	u4HI oFI vI II nlaIII TG CCATCATGGT AC GGTAGTACCA	real csp61 scal CAAGTACTTC
hae aluI mcr rmal eag mae! eae bfal cfr nhe! b811 cac8! msp! alu! hpa! CAAAAAGCTA GCTTATCCGG	fnu4HI bsoFI bbvI nspBII aclI rcccccrG C	xmnI asp700 GGACGAGTT CCTTGCTCAA
	fnu4HI bsoFI bsoFI bsoFI csal csp61 scfl mnll acil nlaIII gtAccGcCTA TAGAGGATTTT ATCCCGGTG CCATCATGGT CATGGCGGAT ATCTCGCTAT TCTCCTAAAA TAGGGCGAC GGTAGTACCA	
rmal macI styl btyl bsaJI blnI avrII[dam-] haeIII/palI stul mnll bfaI TTTGGAGGC TAGGCTTTTG	'AGAGCGATA A	haelli/p hael scrFl mval bs ecoRII dsav bstNI ac apyl[dcm+] bsaJl mnll CCTACCCTG CCTC
	acil rsai csp6i scfi GTACCGCCTA 7 CATGCCGAT 7	haeIII/palI haeI scrFI wval bsrBI ecoRII dsav bsrNI apyI[dcm+] bsal bsaJI mnlI ddeI GGGATTGGCA AGAACGAGA CCTACCCTGG CCTCCGCTCA CCCTAACCGT TCTTGCCTCT GGATGGGACC GGAGGCGAGT
mnli mnli bseRI AGAAGTAGTG AGGAGGCTTT	maell AGTGACGTAA TCACTGCATT ^splice	bsmAI bsaI GGGATTGGCA AGAACGGAGA CCCTAACCGT TCTTGCCTCT
	CCGTGCCAAG	pÉlMI beli Y CCAAAATATG GGTTTTATAC
fnu4HI baoFI bglI sf1I haeIII/palI mnlI mnlI ddeI mnlI bsaJI acil haeIII/palI TATGCAGAGC CCGAGCCGC TCGGCCTCT GAGCTATTCC	tfii hinfi acii thai fnuDiI/mvni bstUi bsh1236i cGCGGATTCC CCGTGCCAAG	pilMI bsli tcaccattg aactgcatcg tcgccgtgtc ccaaaatatg agctggtaac ttgacgtagc agcggcacag ggtttatac
fnu4HI bsoFI bsoFI bglI sfiII sfiII haeIII/palI mnlI haeIII/palI bsaJI mnlI bsaJI acil h		efani Aactgcatcg Ttgacgtagc
fnu4HI bsoFI bsoFI sf1I sf1I haeIII/palI mnll mnll ddeI mnll bsaJI mnll aluI mnll bsaJI acil haeIII/palI antCCAGGCCGC CTCGGCCTCT GAGCTATTCC ATACGTCTCC GGCTCCGGCG GAGCCGAGA CTCGATAAGG	scrFI nc11 hpall dsaV caull GGCCTTGCC ACGTAACCTT	tagi TCGACCATTG AGCTGGTAAC
301	01	ч

#### FIG. 48B

ahalll/dral 701 AGACAGAAT TAATATAGIT CTCAGTAGAG AACTCAAAGA ACCACCACGA GGAGCTCATT TTCTTGCCAA AAGTITGGAT GATGCCTTAA GACTTATTGA TCCTGTCTTA ATTATATCAA GAGTCATCTC TTGAGTTTCT TGGTGGTGCT CCTCGAGTAA AAGAACGGTT TTCAAACCTA CTACGGAATT CTGAATAACT tru91 601 CAMAGAATGA CCACAACCTC TTCAGTGGAA GGTAAACAGA ATCTGGTGAT TATGGGTAGG AAAACCTGGT TCTCCATTCC TGAGAAGAAT CGACCTTTAA mseI GITICTIACT GGTGTTGGAG AAGTCACCTT CCATITGTCT TAGACCACTA ATACCCATCC TITIGGACCA AGAGGTAAGG ACTCTTCTTA GCTGGAAATT aflii/bfri ddel mboli tagi tru9I hinfi foki sfani msei apyI[dcm+] betXI dsav betni **BexAI** hgiAI/aspHI ecl136II **bsp1286 DSIHKAI** hgiJII mnll aluI besSI banII bmyI sstI saci ball backi hinfi hphi alwNI [dcm-] tfil ear1/ksp6321 eco571 Iloqu asel/asnl/vspl mnll tru91 mseI

ecoRII

BCrFI

mval

FIG. 48C

TGIIGGCCII AACCGIICAI IICAICIGIA CCAAACCIAI CAGCCICCGI CAAGACAAAT GGICCIICGG IACTIAGIIG GICCGGIGGA AICIGAGAAA

801 ACAACCGGAA TIGGCAAGIA AAGIAGACAI GGITIGGAIA GICGGAGGCA GIICIGITIA CCAGGAAGCC AIGAAICAAC CAGGCCACCI IAGACICIIT

mnlI

accI nlallI

hpall braWI

Idem

hinfi ddeI pleI

apyl[dcm+] hinfl apyl[dcm+]

betNI

nlalii

betni

ecoRII

dsav

tfil

dsav

ecoRII

BCLFI

BCLFI

mvaI

haeIII/palI

haeI

mnlI ball ddel 901 GIGACAAGGA ICAIGCAGGA AITIGAAAGI GACACGIITI ICCCAGAAAI IGATIIIGGG AAAIAIAAAC CICICCCAGA AIACCAGGG GICCICICG CACIGIICCI AGIACGICCI IAAACIIICA CIGIGCAAAA AGGGICIIIA ACIAAACCC IIIAIAIIIG GAGAGGGICI IAIGGGICG CAGGAGAGAC ecoNI mnlI apyI[dcm+] ecoRII SCIFI bsaJI betNI nval dsav mn l I maell aflili maelii mbol/ndell[dam-] maeIII alwi[dam-] apoi dpnII[dam-] dpnI[dam+] nlaIII 8au3AI

ahall/beaHI

hinli/acyi

hqaI

1001 AGGICCAGGA GGAAAAAGGC AICAAGIAIA AGIITGAAGI CIACGAGAAG AAAGAIAA AGGAAGAIGC IIICAAGIIC ICIAAAGII ICCAAGGICCI CCIIIIIICCG IAGIICAIAI ICAAACIICA GAIGCICIIC IIICIGAIIG ICCIICIACG AAAGIICAAG AGACGAGGG AGGAIIICGA mnlI Iloqu \*END DHFR sfani Ilodm accI BfaNI apyI[dcm+] Ilum ecoRII betNI BCLFI dsav mva] Bau96I avall abuI

beaJI BtyI

Bau3AI

nlaIII

styl ncol

ppu10I

mbol/ndell[dam-] dpnII(dam-) dpnI[dam+]

tru9I msel

aluI fnu4HI **b**BoFI

> betYI/xhoII alwI[dam-] cacel dsal bsmFI beaJI

1101 ATGCATTIT ATAAGACCAT GGGACTTITG CTGGCTTTAG ATCCCCTTGG CTTCGTTAGA ACGCAGCTAC AATTAATACA TAACCTTATG TATCATACA TACGTAAAAA TATTCTGGTA CCCTGAAAAC GACCGAAATC TAGGGGAACC GAAGCAATCT TGCGTCGATG TTAATTATGT ATTGGAATAC ATAGTATGTG asel/asnl/vspl bbvI nsil/avalil

196nee

avall .. aBuI

ecoRII BCLFI INVE

FIG. 48D

	I	H G 5F
ppol apl06 dam-] rrgaart	scrFI mval fnu4HI ecoRII daaV batNI bsoFI apyl[dcm+] hael bbvI acil haelI/pall TCTGGCGGTG GCTGGTGCA AGACCGCCAC GGACCACGT S G G L V Q scrFI ncil mapl	scrFI mvaI ecoRII dsaV bstNI apyI[dcm+] eIII/palI sau96I ecool09I/draII iI asuI rAA GGGCTGGAA ATT CCGGACCTT K G L E
ecoRI taqI apo clai/bsp106 bspDI[dam-] rAT CGATTGAA NTA GCTAACTT	- H 0 0 0	firephi fpsphi is scri is dsa' is dsa' is dsa' is anyi (dcm+ haelli/pali haelli/pali ali sau96i drali sau96i Graf GGCCT
I CGGTTC GCCAAGI	hae acii ha TCTGGCGTG AGACCGCCAC B G G G acrfi ncii	npail dsav cauli smal smal smal scrfi ncil dsav cauli bsali bsali bsali baali haelil/pali asul bsli cccccccrr
mnll beaJI GCACC TC CGTGG AG		npail dsav caulI xmal/pspAl smal smal smal scrFI ncil dsav caulI bsil bsall bsall bsall bsall bsall caulf bsall bsall sau961 haell/pall iV asu1 bsl ecool091/drall GTCCGTCAGC CCCCGGTAA CAGGCACTC.GGGCCCATT V R Q A P G K
(+) Caact Gttga K6G42	rmal mael bfal alul sh GCTAG ST CGATC	I BE II
dsav bstNI apyl[dcm+] mnlI c] bsaJI CTCCCAGGTC CAACTGCACC TCGGTTCTA: GAGGGTCCAG GTTGACGTG AGCCAAGATI seq from pRK6G425VH: Cla-AvrII	CAGAAGTTCA GTCTTCAAGT E V Q	sau96I avaII as nla bsrI TATGCACTGG
dsav tagi apol bstNi tagi apol apol apyl dcm+) mnli clai/bspl06 cAGGTGTCCA GTCCCAGGTC CAACTGCACC TCGGTTCTAT CGATTGAATT GTCCAGT GACCAACTGA GCCAAGATA GCTAACTTAA GCTCAACTTAA GCTCAACTTAA GCTCAACTTAA GCTCAACTTAA GCTCAACTTAA GCTCAACTTAA GCTCAACTTAA GCTCAACTTAA GCTCAACTTAA GCTCACTTAA GCTCACACTTAA GCTCACACTTAA GCTCACTTAA GCTCACACTTAA GCTCACACTAA GCTCACACTAA GCTCACACACTAA GCTCACACACACACACACACACACACACACACACACACAC	### ##################################	pleI hinfI taqI xhoI paeR7I avaII avaII avaII nla paeR7I TACTCCTTCT CGAGTCACTA TATGCACTGG ATGAGGAAGA GCTCAGTGAT ATAGGTGACC Y S F S S H Y H H W FIG. 48E
TTTCTCTCCCA (	bpm] bsrI AACTGCAACT TTGACGTTGA	
CCACTTTGCC	rmal mael bfal TTCTAGTAGC AAGATCATCG	hgiJII bsp1286 bmyI scrFI mval banII ecoRII dsav bstNI
foki ragataacat ktctattgta	foki atcatcettt tagtaggaaa	Blui Blwii   dcm fnut) bsof bbvi TGTCCTGTGC A ACAGGACACG T
mmelli hphi scfi foki GGTGACACTA TAGATAACAT CCACTGTGAT ATCTATTGTA	nlalli NTGGTCATGT	I B6 TCACTCGTT AGTGAGGCAA S L R L
ATACGATITA G TATGCTAAAT C	nlalli styl pflMi ncol dsal bsll fokl bsall fokl GGGGTACCC	hgiJii bep1286 bmyi scrfi mval bmil ecoRii dsaV bstNi bsaJi apyi(dcm+) gccAGGGGC TCACTCCGTT CGGTCCCCG AGTGAGGCAA p G G S L R L
1201 AT TA	1301 CC 1	1401

thal fnuDil/mvnl bstUi bsh1236I nrul TATCTCGCGA CAACTCCAAA AACACACAT ATAGAGCGCT GTTGAGGTTT TTGTGTCGTA	hinli/acyl ahail/baahi beri aatii maeili taqi hphi mboli maeii cAATGGTGAC TGGTTCTTCG ACGTCTGGGG	BCLFI  mval  baayl baayl batni haelil/pall  asui  I bapl286 haelil/pall  asui  nli bspl286 bspl286 acii bsayl  c TCCAAGAGCCCC GTGTCCCGG  G AGGTTCTCGT GGAGACCCC GTGTCCCGG  S K S T S G G T A A
bali sau3Ai mbol/ndeII[dam-] mbol/ndeII[dam-] dpnI[dam+] dpnII[dam-] lbnII[dam-] lbnII[dam	beti ball/bahli beti autii beti begi caceli didi dedi didi actic concordede concordece c	sau961  nla1V  hglois  esp31  bsp1286  ban1  mval  bsp1201  mval  bsp1201  mval  bsp1201  bsp1201  mval  bsp1201  bsp1201  bsp1201  bsp1201  bsp1201  bsp1201  bsp11 hphi  bsp11 hphi  bsp11 haelil/pali  ccGGCCATCCCCTCCTCCCTCCTCCTCCTCCTCCTCCCCCCCC
bali sau3Ai mbol/ndeli[dam-] dpni[dam+] dpnil[dam-] alwi[dam-] hphi alwi[dam-] ACCAACCTA ATATTGATCC, TTCCAATGGT ACCCAACCTA TATAACTAGG AAGGTTACCA	scfi psti bsgi cac81 mnli bspMi cac81 ddel drdi 1601 ACCTGCAGAT GAACAGCCTG CGTGCTGAGG AC TGGACGTCTA CTTGTCGGAC GCACGACTCC TG	esp31 mval bsmBI ecoRII dsav bstNI hphI mnlI apyI(dcm+) bsaJI bsaJI maeIII bseRI m nlaIV bstEII bsmAI hae 1701 TCAAGGAACC CTGGTCACG TCTCCTCGG AGTTCCTTGG GACCAGTGGC AGAGGAGCCC 114 Q G T L V T V S S A

hinpi nlaiv nari bapi286 kasi baiHKAi mapi hjici cac8i hpali haeli baofi acil apali/snol daav ddel hhal/cfol napBii alw441/snol cauli GAACTCAGGC GCCCTGACCA GCGCGTGCA CACCTTCCCG CTTGAGTCG CGCGACGT GTGAAGGCC CGACAGGATG N S G A L T S G V H T F P A V L Q	tfil hinfi maeli IA CATCTGCAAC GTGAATCACA AGCCCAGCAA AT GTAGACGTG CACTTAGTGT TCGGGTCGTT I C N V N H K P S N ahdi/eamil05i aau96i	eccri mval mval ecoRII dsavl r bstNl r bsavl k dcm-] apyl[dcm CCTGAACTCC TGGG GGACTTGAGG ACCC
hinpi nlalv nari hphi hphi mspl hpali cfrlol/bsrFi bsawi age! tthlill/aspl ddel hhal/cfol nsp carcect ccacacac ctrongc ccctcac ctroccac cccacacac E p v T v S w N S G A L T S	fnu4HI bsoFI nlaIV  ImaI hg1CI  bsp1286 macI banI  hphI bfaI aluI bsp1286  hphI bmyI mnlI bbvI bmyI  TGGTGACTGT GCCTCTAGC ACCTTGGCAAAC GTGAATCACA AGCCCAGAAA  ACCACTGAAC GGGAGATCG TCGAACCGT GTAGACGTTG CACTTAGTGT TCGGGTCGTT  ACCACTGACA CGGAGATCG TCGAACCGT GGTCTGGAT GTAGACGTTG CACTTAGTGT TCGGGTCGTT  ACCACTGACA CGGGAGATCG TCGAACCGT GGGTCTGGAT GTAGACGTTG CACTTAGTGT TCGGGTCGTT  ACCACTGACA CGGGAGATCG TCGAACCGT GGGTCTGGAT GTAGACGTTG  ACCACTGACA AGCCCAGACCAAA AGCCCAGCAAA  ACCACTGACA AGCCCAGACAAA  ACCACTGACACAAA AGCCCAGAAAAAAAAAAAAAAAAAA	nlalli napli napli ATCTTGTGAC AAAACTCACA CATGCCCACC TAGAACATG TTTTGAGTGT GTACGGGTGG S C D K T H T C P P
BCTFI mval ecoRII ecoNI deav betNI bell apyI[dcm+] fnu4HI bsoFI bboVI 1801 CTGGCTGCC TGGTCAAGGA CTACTTCCCC GACCGACGG ACCAGTTCCT GATGAAGGGG	ddel plei fnu4HI mnli hinfi bsoFi eco8ll mnli bbvi bsu361/mstII/saul ddel 1901 AGTCCTCAGG ACTCTACTCC CTCAGCAGCG TCAGGAGTCC TGAGATGAGG GAGTCGTCGC 181 S S G L X S L S S V	hgiJII beaJI beaJI benJI meli banII 2001 CACCAAGGGG GACAAGAAAG TIGAGCCCAA GIGGTICCAC CIGTICITIC AACTCGGGT

N N

S

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bsu36I/mstII/sauI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         baoFI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          bbvI
   eari/kap6321 baaJi mali bapHi[dam-] asui bau361/mstii/saui maeli bbai bau361/matii/sa
                                     GAGAAGGGGG GITTIGGGTT CCTGTGGGAG TACTAGAGG CCTGGGGACT CCAGTGTACG CACCACCAC TGCACTCGGT GCTTCTGGGA CTCCAGTTCA
                                                                                                                                                                                                                                                                                                                2201 TCAACTGGTA CGTGGACGGC GTGGAGGTGC ATAATGCCAA GACAAAGCCG CGGGAGGAGC AGTACAACAG CACGTACCGT GTGGTCAGĆG TCCTCACCGT
                                                                                                                                                                                                                                                                                                                                 AGTIGACCAI GCACCIGCCG CACCICCACG TAITACGGIT CIGITICGGC GCCCICCICG TCAIGITGIC GIGCAIGGCA CACCAGICGC AGGAGIGGCA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   2301 CCTGCACCÁG GACTGGCTGA ATGGCAAGGA GTACAAGTGC AAGGTCTCCA ACAAAGCCCT CCCAGCCCCC ATCGAGAAAA CCATCTCCAA AGCCAAAGGG
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    GGACGTGGTC CTGACCGACT TACCGTTCCT CATGTTCACG TTCCAGAGGT TGTTTCGGGA GGGTCGGGG TAGCTCTTTT GGTAGAGGTT TCGGTTTCCC
                                                                                                                                                                                                                                                                                                                                                                             V V S V L T V
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mboll ddel
                                                                                   ED
                                                                        A S V G V V
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                                                                                                                                                                                                                                                                                              Cap6I
                                                                                                                                                                                                                                                                              rBaI
                                                                                                                                                                                                                                                                                                             maell
                                                                                                                                                                                                                                                                                                                                                                        Y N S
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                                                                                                                                                                                                                                                                                                          real
                                                                  T P E V T C
                                                                                                                                                fnuDII/mvnI
 eco811 maeIII
                                                                                                                                                                                                Sacil/sstil
                                                                                                                                                                                                                                                                                                       mnlI
                                                                                                                                                                                    beh1236I
                                                                                                                  acil
                                                                                                                                                                                                                    nspBII
                                                                                                                                                                   bstul
                                                                                                                                  thaI
                                                                                                                                                                                                                                                                                                    fnu4HI
                                                                                                                                                                                                                                                                     baaJI
                                                                                                                                                                                                                                    kapi
                                                                                                                                                                                                                                                   daaI
                                                                                                                                                                                                                                                                                     acli
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 dpnII(dam-)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                    rsaI
                                                                                                                                                                                                                                                                                                             mn]I
                                                                                                                                                                                                                                                                                                                                                                                                                                                        ecoNI batNI barI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                         apyI[dcm+]
                                                                                                                                                                                                                                                         maeII
                                                                                                                                                                                                                                                                                                     berI beall
                                                                                                                                                                                                                                                                                       csp6I
                                                      247 L F P P
                                                                                                                                                                                                                                                                                                                                                                                                                          ecoRII
                                                                                                                                                                                                                                                                        real
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                                                                                                                                                                                                                                                                                                                                                                                                          mvaI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                          ball
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drdl

nlaIII

IHdau

mnlI

malI

ddeI

nspI

mbol/ndell[dam-]

Cauli

nlaIII

rcal dpn1[dam+]

mn]I

Iloqu

avall

Bau3AI

dsav ncil

Bau96I

nlaiv

hpall

Idam BCrFI

2401 CAGCCCCGAG AACCACAGGT GTACACCCTG CCCCCATCCC GGGNAGAGAT GACCAAGAAC CAGGTCAGCC TGACCTGCCT GGTCAAAGGC TTCTATCCCA GICGGGGCIC ITGGIGICCA CAIGIGGGAC GGGGGIAGGG CCCIICICIA CIGGITCIIG GICCAGICGG ACTGGACGGA CCAGITICCG AAGAIAGGI T C L V K G apyI[dcm+] **betni** mval bspMI ecoRII O V S L apyI[dcm+] ecoRII **b**BtNI BCFFI **BexAI** JBBV mvaĬ z × bspl4071/bsrGI bslI aval ear1/ksp6321 E E ball bead mboll Cauli BCLFI daav nclI PPSR BMaI fokI CapéI

xmal/pspAI

caull

hpaII

BCLFI

ncil Idem dsaV

nlalv mboli scfi cac8] 2501 GCGACATCGC CGTGGAGTGG GAGAGCAATG GGCAGCCGGA GACAACTAC AAGACCACGC CTCCCGTGCT GGACTCCGAC GGCTCCTTCT TCCTCTACAG CGCTGIAGCG GCACCTCACC CTCTCGTTAC CCGTCGCCT CTTGTTGATG TTCTGGTGCG GAGGGCACGA CCTGAGGCTG CCGAGGAAGA AGGAGATGTC D A V E W E 8 N G O P E N N Y K T T P P V L D S D G 8 F F L Y S D I A V E W E 8 N G O P E N N Y K T T P P V L D S D G 8 F F L Y S mull hinfi pleI mnll hpall MapI fnu4HI baoFI bbvI berDI mell beadI dsal bell

7 7

**>** О а

347 Q P R E

earI/kso6327 mboll mull Bapl sfaNI mnll nsil/avalll nlalII ppu101 nlaIII Ilodm bpuAI XmnI bbsI maeII asp700 fnu4HI **DBOFI** Lvdd IMqad deal

hphI

2601 CAAGCICACC GIGGACAAGA GCAGGIGGCA GCAGGGGAAC GICTICICAI GCICGGIGAI GCAIGAGGCI CIGCACAACC ACIACACGCA GAAGAGCIIC GITCGAGIGG CACCIGITCI CGICCACCGI CGICCCCIIG CAGAAGAGIA CGAGGCACIA CGIACICCGA GACGIGITGG IGAIGIGCGI CIICICGGAG A T H N H H E A S < VFSC N N VDKS alul bsaJI

#### FIG. 48I

maelli Aatggttaca ttaccaatgt	nlalii alwi[dam-] ATCATGTCTG TAGTACAGAC	
aluI fnu4HI bsoFI bbvI GCAGCTTAT	aatgtatctt Itacatagaa	
taqI fnu4HI asuI ncii ncii mspi mael hincii/hindii sfii styi styi alui fnu4HI asuI bhail sii styi styi alui hpail sau96i hinfi psti ciri dsai bsoFi bsoFi bsoFi bsoFi bsoFi bsoI cccTCTCTC CGGGTAAATG AGTGCGACG CCCTAGAGTC GACCTGCAGA AGCTTGGCG CCATGGCCCA ACTTGTTTAT TGCAGCTTAT AATGGTTACA AGCTTGGCG CGTACCGG CGTACCGG CGTACCGG TGAACAAATA ACGTCGAATG TTACCAATGT AATGGTTACA TTACCAATGT AGGACAATGT TACCAATGT TACCAATAATAATAATAATAATAATAATAATAATAATAAT	rmal mae! 2801 ANTAAAGCAA TAGCATCACA AATITCACAT TITITCACTG CATTCTAGTT GIGGITTGTC CAAACTCATC AATGIATCIT ATCATGTCTG TIAITICGIT ATCGIAGIGI TIAAAGGIT TAITTCGIAA AAAAAGTGAC GIAAGATCAA CACCAAACAG GITTGAGTAG TIACAIAGAA TAGTACAGAC	
BCLFI  DCII  MSPI  HPAII  BRAI  BRAI  DBII CAUII  2701 TCCCTGTCTC CGGGTAAATG A  AGGACAGAG GCCCATTAC I  AGGGACAGAG GCCCATTAC I	Bfani apo 2801 Aataaagcaa tagcatcaca Ttatttcgtt atcgtagtgt	<pre>gau3AI mbol/ndeII[dam-] dpnI[dam+]</pre>

haeIII/palI

sau96I

FIG. 48J

dpni[dam+] asp710 hhal/cfol nlaili mnli acc651 ddel acii dpni[dam-] ase1/asn1/vsp1 bsaJ1 2901 GATCGATCGG GAATTAATTC GGCGCAGCAC CATGGCTGA AATAACCTCT GAAAGAAGAA CTTGGTTAGG TACCTTCTGA GGCGGAAAGA ACCATCTGTG CTAGCTAGCC CTTAATTAAG CCGCGTCGTG GTACCGGACT TTATTGGAGA CTTTCTCCTT GAACCAATCC ATGGAAGACT CCGCCTTTCT TGGTAGACAC

dsal hacili/pall

hinpi

mbol/ndell[dam-]

haeI

fuu4HI

tagl[dam-] tru9I

DOLEI mcrI

dpnII(dam-)

pvuI/bapCI

bspDI[dam-] mseI clai/bsp106[dam-]

ZmnX

Bau3AI

bsoFI styI bbvI ncol

csp6I

hgici banI

kpnI

rsal nlaIV

PPU10I PPU10I PPU11I PPU1II PPU1II PPU1II PPU1II PPU1II PPU1II PPU1II PPU1II PPU1II PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIIII PPUIII PPUIIII PPUIII PPUIII PPUIII PPUIIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIII PPUIIII PPUIII PPUII	acii foki ACTCC GCCCATCCG CCCTAACTC FFGAGG CGGGTAGGC	fnu4HI bboFI bboFI bglI haelil/pall mnli mnli ddel mnli mnli mnli mnli mnli baJI mnli alui mnli baJI acii haelil/pall bbeRI cGACTGATTA ANAMATAA ATACGTCTCC GGCTCCGCCCTT GACTATTCC AGAAGTAGTC CGACTGATTA ANAMAATAA ATACGTCTCC GGCTCCGCCG GACCCGAGA CTCGATAGG TCTTCATCAC  FIG. 48K
BfaNI PPU10I nB11/avallI nlallI BPhI nSPI nSPI nSPHI CACSI CATCTATGCA AGCATGCAT CTCA	acii bemfi GTCAGCAACC ATAGTCCCGC CCCT/	fnu4HI bBOFI bBJI sf11 nall haelII/palI mnli mnli mnli bBaJI mnli bBaJI mnli bBaJI mnli bBaJI mnli bBaJI AAAAATAA ATACGTCTCC GGTCCGGCG GAGCC FIG. 48K
BCFFI mval ecoRII dBaV bBtNI apy1[dcm+] bBaJI bBaJI cac8I catacacaca crosscacacacacacacacacacacacacacacacacacac	### scrFI  ### ### ### ########################	fnu4HI bsoFI bsoFI bsoFI styI ncol ncol bsli dsal acti bsaJI acti bsaJI acti bsaJI acti bsaJI acti bsaJI acti bsaJI bsaJI bsaJI bsaJI bsaJI alui bccccangric cccccntrg ccgccccntg cctgcctnt ratering acti ccgcccntr ccgcccntr ccgcccntr and

tfil hinfi acil thai fnuDiI/mvni bstUI bsh1236I CGGGGATTCC CCGTGCCAAG AGTCAGGTAA GCGCCTAAGG GGCAGGTTC TCAGTCCATT U1 matched splice donar^	sau3AI mbol/ndeII[dam-] dpnI[dam+] dpnII[dam-] taqI[dam-] clal/bspl06[dam-] sau3AI mbol/ndeII[dam-] dpnII[dam-] alwI[dam-] trG GAAACCTACTG ACACTGACAT TTG GAAACCTAG CTAGGATGAC TTG GAAACCTAG CTAGGATGAC TTG GAAACCTAG CTAGGATGAC ITG GAAACCTAGI AGAIG ANC CTTTTGGATC GATCCTACTG ANC CTTTTGGATC GATCCTACTG ANC CTTTTGGATC GATCCTACTG ANC GATAGATG ANC GATAGATG Laniat consensus^ Igg vW natural lariat restored^
BCCFI  ncii  mspi halil/pali  asal/xmalil/eclXi easi cfri bsiEi  mspi cauli hpali GCTTATCCG CGGGAACGG TGCATTGGAA AVELI - Hindili frag	fnu4HI bsoFI acil thai thai fnuDII/mvnI tru9I bstUI bstUI aseI/asnI/vspI c GTTAGAACGC GGCTACAATT AATACATAAC G CAATCTTGCG CCGATGTTAA TTATGTATTG
BerFI  mael  mael  mael  mael  styl  bbajl  avili(dam-)  mael  avili(dam-)  mael  avili(dam-)  mael  avili(dam-)  mael  avili(dam-)  mael  cacl  haell/pall  bfal  cacl  mapl cauli  mull  mull  mull bfal  alul  hpall  reg  cacl  reg  cacl  haell/pall  bfal  cacl  hael  cacl  haell  cacl  haell  haell/pall  styl  cacl  haell/pall  haell/pall  cacl  haell  cacl  haell  haell/pall  cacl  haell  haell/pall  cacl  haell  haell/pall  haell/pall  cacl  haell/pall  haell/pall  cacl  haell/pall  bfal  cacl  haell/pall  cacl  haell/pall  bfal  cacl  haell/pall  haell/pall  cacl  haell/pall  bfal  cacl  haell/pall  cacl  haell/pall  cacl  haell/pall  cacl  haell/pall  bfal  cacl  haell/pall  cacl  cacl  haell/pall  cacl  haell/pall  cacl  haell/pall  cacl  c	betXI scil scil styl real pleI hacili/pali csp61 scfl hinfi asul bsaJI GTACCGCCTA TAGAGTCTAT AGGCCACCC CCTTGGCTT CATGCGGAT ATCTCAGATA TCCGGTGGG GGAACCGAA
3301	3401

FIG. 48L

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beteii hphi bepmi hindiii nlaiii beani beii hphi bepmi apyi(dcm+) 3701 atagggtcac catcaccac aggtcaaggaa aagctccgaa
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           TATCCCAGTG GTAGTGGACG TCCAGTTCAG TTTCGAATCA TGTACCATAT CCACGATGCA TAAATGTGAC CATAGTTGTC TTTGGTCCTT TTCGAGGCTT
                                                                                                                                                                                                                                                                                                                                                                    3601 IGSTCATGIA TCATCCTITI ICIAGIAGCA ACTGCAACIG GAGIACATIC AGAIAICCAG AIGACCCAGI CCCCGAGCIC CCIGICGGC ICIGIGGGCG
                                                                                                                                                                                                                                                                                                                                                                                   ACCAGTACAT AGTAGGAAAA AGATCATCGT TGACGTTGAC CTCATGTAAG TCTATAGGTC TACTGGGTCA GGGGCTCGAG GGACAGGCGG AGACACCCGC
                                                                                                             ball foki
                                                                                                                                        3501 CCACITITIC TITITCICCA CAGGIGICCA CTCCCAGGIC CAACIGCACC TCGGIICGCG AAGCIAGCII GGGCIGCAIC GAITGAAITC CACCAIGGGA
                                                                                                                                                     GGTGAAAAG AAAAAGAGGT GTCCACAGGT GAGGGTCCAG GTTGACGTGG AGCCAAGCGC TTCGATCGAA CCCGACGTAG CTAACTTAAG GTGGTACCCT
                                                                                                                             beaJI
                                                                                               dsaI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   aluI
                                      nlallI
                                                               pflMI
                                                                                  ncol
                                                                                                                                                                                                                                                                                                                                                           acti
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                                                                                                ecoRI
                                                                                                                                                                                                                                                                                                                                                                                                                                       BCIFI
                                                                                                            Ioda
                                                                                                                                                                                                                                                                                                                                                                                                                                                       mvaI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    daav
                                                                                                                              bbvI bspDI[dam-]
                                                                                                                                                                                                                                                                hgiAI/aspHI
                                                                                                                                                                                                                                                                                  ec1136II
                                                                                                                 bsoFI taqI
                                                                    claI/bsp106
                                                                                                                                                                                                                                                                                               bap1286
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                                                                                                                                                                                                                                      BacI
                                                                                                 fnu4HI
                                                                                                                                                                                                                                                                                                                                              berI aval
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                                                                                                cacel
                                                        bfal
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                                                                                                     batuI
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                                                                                     fnuDII/mvnI
                                                                       nheI
                                                                                                                                                                                                                                                                                                                                                                                                          a
                                                                                                                                                                                                                                                                                                                                                              ecoRV
                                                                                                                                  beaJI
                                                                                                                    mnll
                                                                                                                                                                                                                                                                                                                                                bpmI/gsuI[dcm-]
                                                                                                                                                                                                                                                                                                                                                               cap6I
                                                                                                                                                                                                                                                                                                                                    real
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        csp6I
                                                                                                                                                                                                                                                                                                                                                                                                                                                                            rsal
                                                                                                                      apy1[dcm+]
Bau96I
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                avall
                              asuI
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C
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#### FIG. 48M

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fnu4HI
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                                                                                                                Ivdd
                                                                                                                                                                                                                                                                                                                                                                                     haeIII/palI
                                                                                                                             BcfI
                                                                                                                                         pstI
                                                                                                                                                        Ibad
                                                                                                                                                                                                                                                                               mbol/ndell[dam-] fnu4HI
                                                                                                             3801 ACTACTGATT TACAAAGTAT CCAATCGATT CTCTGGAGTC CCTTCTCGCT TCTCTGGATC CGGTTTTCA CTCTGACCAT CAGCAGTCTG
                                                                                                                             TGATGACTAA ATGTTTCATA GGTTAGCTAA GAGACCTCAG GGAAGAGCGA AGAGACCTAG GCCAAGACCC TGCCTAAAGT GAGACTGGTA GTCGTCAGAC
                                                                                                                                                                                                                                                                                                       bsoFI
                                                                                                                                                                                                                                                                           3901 CAGCCAGAAG ACTTCGCAAC TTATTACTGT TCACAGAGTA CTCATGTCCC GCTCACGTTT GGACAGGGTA CCAAGGTGGA GATCAAACGA ACTGTGGCTG
                                                                                                                                                                                                                                                                                           GTCGGTCTTC TGAAGCGTTG AATAATGACA AGTGTCTCAT GAGTACAGGG CGAGTGCAAA CCTGTCCCAT GGTTCCACCT CTAGTTTGCT TGACACCGAC
                                                                                                                                                                                                                                                                                                                                                        TVAA
                                                                                                                                                                                                                                                                                                                                                                       4001 CACCATCTGT CTTCATCTTC CCGCCATCTG ATGAGCAGTT GAAATCTGGA ACTGCTTCTG TTGTGTGCCT GCTGAATAAC TTCTATCCCA GAGAGCCAA
GTGGTAGACA GAAGTAGAAG GGCGGTAGAC TACTCGTCAA CTTTAGACCT TGACGAAGAC AACACGGA CGACTTATTG AAGATAGGGT CTCTCCGGTT
                                                                                                                                                                                              S
                                                                                                                                                                                            လ
                                                                                                                                                                                      LTI
                                                                                                                                                                                                                                                                                                                                                    IXR
                                                                                                                                                                                                                                                                       Bau3AI
                                                                                                                                                                              T D F T
                                                                                                                                                                                                                                                                                                                                               X V E
                                                                                                                                                                                                                                                                         banl baaJI
                                                                                                                                                                                                                                              kpnI styI
                                   mbol/ndell[dam:]
                                                                                                                                                                                                                         Cep6I
                                                                                                                                                                                                                                    nlaIV
                                                                                                                                                                                                           rsal
                                                                                                                                                                                                                                                               haici
                                                                dpnII [dam-]
                                                dpnI{dam+}
                                                                           alwI[dam-]
                                                                                                     batYI/xhoII
         beawi
ball
                         6au3AI
                                                                                           nlaiv
                                                                                                                                                                                                                                                                  acil
                                                                                        bpmI/gauI[dcm-]
                                                                                DSmFI
                                                                                                clai/bsp106 pleI
                                                                         hinfi
                                                                                        tagi
                                                                                                                                                                                                                                                                                                                                                                      mboll acil
                                                                                                                                                                                                                                                                                                                                                       DPuAI
                                                                                                                                                                                                                                                                                                                                                                     ppeI
                                                                                                                                                                                                                                                           bpuAI
                                                                                                                                                                                                                                             Iloqu
                                                                                                                                                                                                                                                                        ppeI
```

hpall

Idem

<u>Б</u>

FY

FIG. 48N

```
4101 AGIACAGIGG AAGGIGGATA ACGCCCICCA ATCGGGIAAC TCCCAGGAGA GIGTCACAGA GCAGGACAGC AAGGACAGCA CTACAGCCT CAGCACACC
TCATGICACC TICCACCTAT TGCGGGAGGT TAGCCCATIG AGGTCCTCT CACAGTCT CGICCTGICG TICCTGICGT GGATGICGGA GTCGICGG
                                                                                                                                                                                                                                                                      4301 GAGAGTGTTA AGCTTGGCC CCATGGCCCA ACTTGTTTAT TGCAGCTTAT AATGGTTACA AATAAAGCAA TAGCATCACAAT TCGAACCGGC GGTACCGGGT TGAACAAATA ACGTCGAATGT TTATTTGGTT ATCGTAGTGT TTAAAGTGTT TATTTCGTT ATCGTAGTGT TTAAAGTGTT TATTTCGTA
                                                                                                                            YSL
                                                                                                                                                                                                                                                                                                                                              T X S
                                                                                                                                                                               hgiAI/aspHI
                                                                                                                                                                                            eċll36II
                                                                                                                                                                                                                                        ddel cac81
                                                                                                                                                                                                         bsp1286
                                                                                                                                                                     hglJII
                                                                                                                                                                                                                   DEIHKAI
                                                                                                                                                                                                                                                   haeIII/palI
                                                                                                                                             sstI
                                                                                                                                                           BacI
                                                                                                                                                                                                                                                               Bau96I aluI
                                                                                                                                                                                                                                 DmyI
                        CCORII
SCLFI
                                             batNI
           MVaI
                                   dsav
                                                                                                                                                                                                                                                                                                                                                                                                              aluī
                                                                                                                                                                                                                                                                                                                                                                                                                      fnu4HI
                                                                                                                                                                                                                                                                                                                                                 haeIII/palI
                                               mnll
                                                                                                                                                                                                                                                                                                                                                                Ingo
                                                                                                                                                                                                                                                                                                                                                                    bsoFI nlaIII
                                                                                                                                                                                                                                                                                                                                                                                        aluI haeIII/pall
                                                                                                                                                                                                                                                                                                                                                                              sfil styl
                                                                                                                                                                                                                                                                                                                                                                                                  hindill bgll ncol
                                                                                                                                                                                                                                                                                                                                                                                                                       daal
                                                                                                                                                                                                                                                                                                                                                          fnutHI
                                                                                                                                                                                                                                                      blpI/bpull021
                                                                                                                                                                                                                                                                                                                                                                                                              tru91 eael
                                                                                                                                                                                                                                           cellI/espI
                                                                                                                                                                                                                                ddeI
                                                 Cep61
                                      rsal
                                                                                                                                                                                                                                                                   hqaI
```

FIG. 480

## FIG. 48P

	Sv40 origin  ScrFI  mva: ecoRI	dsav bstni apyl[dcm+] bsaJI ATGTGTGT CAGTAGGGT GTGGAAAGTC CCCAGGCTCC TACACACA GTCAATCCCA CACCTTTCAG GGGTCCGAGG	BCCFI MVAI BCCFI BOUNT B
Eau3An  mbol/ dpnII  pvul/bs  mcri  bstEI  tagl[dam cla1/bsp]  bsmI bfaI  ANAAAGTGAC GTAAGATCAA CACCAAACAG GTTTGAGTAG TTACATAGAA TAGTACAGAC CTAGCTAGCC  Eau3AI  mbol/ndeII  dpnI[dam+]  dpnI[dam+]  ANAAAGTGAC GTAAGATCAA CACCAAACAG GTTTGACGTAGC CTAGCTAGCC  TAGATACAGAC CTAGCTAGCT  ANAAAGTGAC CTAGCTAGCT  ANAAAGTGAC CTAGCTAGCC  TAGATACAACAGAC CTAGCTAGCC  TAGATACAACACACC  TAGATACAACACCC  TAGATACAACACC  TAGATACAACACCC  TAGATACAACACACCC  TAGATACAACACCC  TAGATACACCC  TAGATACACCC	real csp61 nlaIv kpnI hgiCI	### ##################################	Valii CTCAATTAGT GAGTTAATCA

```
apyI [dcm+]
                                                                                                                                                                                                                                                  maeIII
           4701 ATCTCAATTA GTCAGCAACC ATAGTCCCGC CCCTAACTCC GCCCATCCCG CCCCTAACTC CGCCCAGTTC CGCCCATTCT CCGCCCATCT CGCCCCATTCT CGCCCCATCT CGCCCCATCT CGCCCCATCT CGCCCCATCT CGCCCCATCT CGCCCCATCT CGCCCCATCT CGCCCCATCT CGCCCCATCT CGCCCCCATCT CGCCCCCATCT CGCCCCCATCT CGCCCCCATCT CGCCCCCATCT CGCCCCCATCT CACCCCATCATTA
                                                                                                                                                                                                                                                                                                                                                                                                                                   ecoRII
                                                                                                                                                                                                                                                                                                                                                                                                        BCLFI
                                                                                                                                                                                                                                                                                                                                                                                                                                                             bstNI
                                                                                                                                                                                                                                                                                                                                                                                                                                                dsav
                                                                                                                                                                                                          ABADANTATT TATGCAGAGG CCGAGGCCGC CTCGGCCTCT GAGCTATTCC AGAAGTAGTG AGGAGGCTTT TTTGGAGGC TAGGCTTTTG CAAAAAGGTG CCTCGGCG GAGCCGGAGA CTCGATAAGG TCTTCATCAC TCCTCCGAAA AAACCTCCGG ATCCGAAAAC GTTTTGGAGCTG
                                                                                                                                                                                                                                                                                                                                                                                                                     MVaI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        beaJI
                                                                                                                                                                                                                                                                                                                                                                                                                                   ANTGGAGCTC GCCGCCAAT TAATTCCGCG CGCATTTAAA TCCTGCAGGT AACAGCTTGG CACTGGCGGT CGTTTTACAA GGTCGTGAAAACCC
                                                                                                                                                                                                                                                                                            start pucile.
nlaIII
                                                                                                                                                                                       avrII[dam-]
                                                                                                                                                                                                   haeIII/palI
                                                                                                                                    MaeI
                                                                                                                                                             bsaJI
                                                                                                                      rmal
                                                                                                                                                                            blnI
                                                                                                                                                 styl
                                                                                                                                                                                                                                                                                                                                                                                                                         haeIII/pall
                                                                                                                                                                                                                                                                                                                                                                                  PspMI
                                                                                                                                                                                             haeIII/palI bsaJI mnlI aluI
                                                                                                                                                                                                                                                                                                                                                                                                                pstI
                                                                                                                                                                                                                                                                                                                                                                                                   scfI
                                                                                                                                                                                                                                                                                                                                                                                                                      ahalll/dral
                                                                                                                                                                                                                                                                                                                                                                                                           tru9I
                                                                                                                                                                                                                                                                                                                                                                                                                        meel trus: bah1236I msel
                                                                                                                                                                                                                                                                                                                                             fuuDII/mvnI
                                                                                                                                                                                                                                                                                                                   hhaI/cfoI
                                                                                                                                                                       haeIII/pall
                                                                                                                                                                                                                                                                                                                                                                                      hhaI/cfoI
                                                                                                                                                                                          mnll
                                                                                                                                                                                                                                                                                                      hinpr
                                                                                                                 fnu4HI
      acil
                                                                                                                                                                                                                                                                                                                                                             batul
                                                                                                                               bsoFI
                                                                                                                                                                                                                                                                                                                                                                                                     CacBI
                                                                                                                                                                                                                                                                                                                     eagl/xmall1/eclXI thal
                                                                                                                                              pglI
                                                                                                                                                                                                                                                                                                                                                                        hinpi
                                                                                                                                                            sf1I
                                                                                                                                                                                                                                                                                                                                                                                                                    ascī
                                                                                                                                                                                       Mnll
                                                                                                                                                                                                                                                                                           haelli/pall
                                                                                                                                                                                                                                                                                                                                                                                                tru91
                                                                                                                                                                                                                                                                                                                                                                                                    paeR71 bsiEI pacI
                                                                                                                                                                                                                                                                                                                                                             barBI baoFI
                                                                                                                                                                                                                                                                                                                                       eael
                                                                                                                                                                                                                                                                                                                                                                                       xhoI fnu4HI
                                                                                                                                                                                                                                                                                                                                                                              cfrI
                                                                                                                                                                                                                                                                                                                                                                                                                      aval bsoFI
                                                                                                                                                                                                                                                                                                                                                                             tagi
```

FIG. 48Q

```
funDII/mvnI
                                        5001 TGGCGTTACC CNACTTAATC GCCTTGCAGC ACATCCCCC TTCGCCAGCT GGCGTAATAG CGAAGAGGCC GGCACGATC GCCTTCCCA ACAGTTGCGT GCGAATGG GTTGAATTAG CGAACGTCG TGTAGGGGG AAGGGGTCGA CCGATTATC GCTTCTCCGG GCGTGGCTAG CGGGAAGGGT TGTCAACGCA
                                                                                                                                                                                                 batul acfi
                                                                                                                                                                                                                       rsal hhal/cfol
                                                                                                                                                                                               5101 AGCCTGAATG GCGAATGGCG CCTGATGCGG TATTTTCTCC TTACGCATCT GTGCGGTATT TCACACCGCA TACGTCAAAG CAACCATAGT ACGCGCCTG
TCGGACTTAC CGCTTACCGC GGACTACGCC ATAAAAGAG AATGCGTAGA CACGCCATAA AGTGTGGCGT ATGCAGTTTC GTTGGTATCA TGCGCGGGAC
                                                                                                                                                                                                                                                                                                                                                        hinpi
                                                                                                                                                                              thaI
mbol/ndell[dam-]
                                  dpnII (dam-)
            dpnI(dam+)
                   haeIII/palI
                                                                                                                                                                                                                                                                                                                         hhal/cfol
                                                                                                                                                                                                                                                                                                               hinpi
                                                                                                                                                                                                                                                                                                                                             hinpi haeii
                                Insp
                                                                                                                                                                                                                                                                                                                                       IDE
            cac8I
                      aluI
                                  IInad
                                                                                                                                                                                                                                                                                                                                fnuDII/mvnI
                                                                                                                                                                                                                                                                                                        hhaI/cfoI
                                                                                                                                                                                                                                                                        fnu4HI
                                                                                                                                                                                                                                                                                   bsoFI
                                                                                                                                                                                                                                                                                                                                                     bsh1236I
                                                                                                                                                                                                                                                                                              hinpr
                                                                                                                                                                                                                                                                                                                                             bstur
                         fnu4HI
                                   bsoFI
                                                                                                                                                                                         BfaNI
                                                                                                                                                 hinli/acyi
                                                                                                                                                                                                                                                                                            fnuDII/mvnI
                                                                                                                  nlaIV
                                                                                                                                                                                                                                                                                                                                 hhaI/cfoI
                                                                                                                                                                                                                                                                                                                                                      msel bshl236I
                                                                                                                                                                           haell
                                                                                                                                                               hgici
                                tru91
                                                                                                                             narī
                                                                                                                                        kabi
                                                                                                                                                                                                                                                                          DSOFI
                                                                                                                                                                                      banı
                                                                                                                                                                                                                                                                                                          bstuI
                                                                                                                                                                                                                                                                                   thal
                                                                                                                                                                                                                                                                                                                                           tru91 ac11
                                                                                                                                                                                                                                                                                                                 hhal/cfol hinpl
                                                                                                                                                                                                                                                                                                      hinpi
                                                                                                                                                                                                                                                                                                                             fnu4HI
                                                                                                                                                                                                                                                                                                                                          DBOFI
```

FIG. 48R

# FIG. 48S

V I B6 nlalv hglCI tag1 CCCTTTAGG TTCCGATTTA GTGCTTTAGG GCACTCGAC	ATAGACGGTT TTTCGCCCTT TGACGTTCGACTC GGGTTTTTG  ATAGACGGTT TTTCGCCCTT TGACGTTCGA GTCCACAAAAAC  TATCTGCCAA AAAGCGGGAA ACTGCAACCT CAGGTGCAAG AAATTAATAGTG GACTCTTGTT	tru9I  mseI  GCCTATTGGT TAAAAAATGA GCTGATAAA  CGGATAACCA ATTTTTAA	hgiAl/aspHI bspl286 bsilkAl bmyI ddeI apaLI/snoI rsaI bsoFI tru9I alw441/snoI csp6I sfaNI mseI GTGCACTCTC AGTACAATCT GCTCTGATGC CGCAAAGTTA acii	BfaNI mspI hpaII scrFI nciI dsav fokI cauli acii
nlalv hglJII bsp1286 bmyI banII NA ATCGGGGCT CCCTTTAGGG TTCCGATTT	""  ""  ""  ""  ""  ""  ""  ""  ""  ""	T TTTGATTTAT AAGGGATTTT GCCGATTTCG A AAACTAAATA TTCCCTAAAA GGCTAAAGC	hgiAl/aspHI bsp1286 bslHKAl bmyl ddel apaLl/snol rsal alw441/snol csp61 GTGCACTCTC AGTACAATCT	hinpi hhal/cfol thal thal thal fubli/mvni bstul bstul cccccAACAC GCGCCAACAC GCGCTGACGC GCCCTGACGG GCTTGTCTGC TCCCGCTAACACACACACACGC GCCCTGACGG GCTTGTCTGC TCCCGCAACACACACGC GCCCTGACGG GCTTGTCTGC TCCCGCAACACACACGC GCCTGACGC GCCTGACGC GCCTGACGC GCCTGACGC GCCTGACGC GCCTGACGC GCCTGACGC GCCTGACGC GCCTGACACACACACACACACACACACACACACACACACA
mspI hpaII naeI cfr101/bsrFI 5301 TTTCTCGCCA CGTTCGCCGG CTTTCCCCGT CAAGGGGCT AAAGAGCGGT GCAAGGGGCC GAAAGGGGCA GTTCGACGTT TAGCCCGA	maeli haelii/pali ' draii sau96i bsaAi sau1 AACTAATTTGG TGATGGTTCA GGTAGTGGC CATCGCCCTG ATAGACGGTT TTTCGCCCTT AACTAAACCC ACTACCAAGT GCATCACCG GTAGCGGAC TATCGCCAA AAAGCGGGAA	bsrI bsrI bslI ccanacreda acaacacrea accepatere eccanare trugi eccanacreda acaacacrea accepatere eccanare trugi eccanacreda accepatere eccanare trugitarian and trecepana eccanare alui msel msel ectatere retreser tregende eccanare and anchara trecepana eccanare eccanare eccanare eccanares.	thai fnuDII/mvni tru91 apol tru91 psp14061 msel bstuI msel tru91 5601 CAAAATTA AGGGGAATTT TAACAAAATA TTAAGGTTAA GTTTTTAAAT TGGGTTAAA ATTGTTTTAT AATTGCAAAT	hinpi maelii baori baori bari nlalli hhal/cfoi 5701 GCTATCGCTA CGTGACTGGG TCATGGCTGC GCCCCGACAC CGATAGCTGG CATAGGTGC GCCCCGACAC GGATAGCGGC CGGGCTGG CGGGGCTGG CGGGCTGG CGGGCTGTG CGGGCTGG CGGGCTGTG CGGGCCTGTG CGGGCTGTG CGGGGCTGTG CGGGGCTGTG CGGGCTGTG CGGGGCTGTG CGGGGGGGG

```
hgiAI/aspHI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         alw441/snol
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             apaLI/snoI
                                                                                                                    haeIII/pall
                                                                                                                                                          eco01091/drall
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        bsp1286
                                                                                                   alui bali cauli alui nialli mnii npni npni banizsbi bbal ecolloyl/drali ecolloyl/drali ecolloyl/drali
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     DB1HKAI
                                                                                                                        GTTCGACACT GGCAGAGGCC CTCGACGTAC ACAGTCTCCA AAAGTGGCAG TAGTGGCTTT GCGCGCTCCG TCATAAGAAC TTCTGCTTTC CCGGAGCACT
                                                                                                                                                                                                                                                                                       ATGCGGATAA AAATATCCAA TTACAGTACT ATTATTACCA AAGAATCTGC AGTCCACCGT GAAAAGCCCC TTTACACGCG CCTTGGGGAT AAACAAATAA
                                                                                                                                                                                                                                                                     5901 TACGCCTATT TTTATAGGTT AATGTCATGA TAATAATGGT TTCTTAGACG TCAGGTGGCA CTTTTCGGGG AAATGTGCGC GGAACCCCTA TTTGTTTATT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            mbol/ndell[dam-]
                                                                                                                                                                                                                                                                                                                                                                        AAAGATTTAT GTAAGTTTAT ACATAGGGG GTACTGTT ATTGGGACAA TTACCTTCA ATAATATTGA AAAAGGAAGA GTATGAGTAT TCAACATTTC
AAAGATTTAT GTAAGTTTAT ACATAGGGG GTACTCTGTT ATTGGGACTA TTTACGAAGT TATTATAACT TTTCCTTCT CATACTCATA AGTTGTAAG
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          dpn1[dam+] bmy1
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                GCACAGCGCG AATAAGGGAA AAAACGCCGT TITTGCCTTC CTGTTTTTGC TCACCCAGAA ACGCTGGTGA AAGTAAAAGA TGCTGAAGAT CAGTTGGGTG

GCACAGCGGG AATAAGGGAA AAAACGCCGT AAAACGGAAG GACAAAAAAGA AGTGGGTGTT TGCGACCACT TTCATTTTCT ACGACTTCTA GTCAACCCAC
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               Bau3AI
                                                                                                                                                                                                                                                        fnuDII/mvnI
                                                                                                                                                                                                                 nlaIV
                                                                                                                                                                                                                              acti
                                                                                                                                                                                                                                           thaI
                          fnuDII/mvnI
                                                      bBh1236I
                                                                                hhal/cfol
                                                                                              thal mull
                                        bstul
                                                                    hinpi
                                                                                                                                                                                                                                                               ahall/bsalll
                                                                                                                                                                                                                                                 hinli/acyi
                                                                                                                                                                                                                                                                                                                                                                      bemAI
                                                            IHdgu
                                                                                                                                                                                                                                                   nlaIII
                                               Ideu
                                                                      fnu4HI
                                                                                                                                                                                                                                                                                                                                                                   berBI
                                                                                       bsoFI
                                                                                                                                                                                                                                                                   rcal
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                fnu4HI
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              bBoFI
                                                                                                                                                                                                                                                              tru91
BCLFI
                                         hpaII
            ncil
                           Idem
                                                      daav
                                                                                       maelli bamAl
                                                                 esp3I
                                                                               DemBI
```

FIG. 48T

GIGCICACCC AAIGIAGCII GACCIAGAGI IGICGCCAII CIAGGAACIC ICAAAAGCGG GGCIICTIGC AAAAGGIIAC IACICGIGAA AAITICAAGA 6201 CACGAGIGGG TIACAICGAA CIGGAICICA ACAGCGGIAA GAICCIIGAG AGIITICGCC CCGAAGAACG IITICCAAIG AIGAGCACII IIAAAGIICI ahalll/dral bsp1286 tru91 mseI hqiAI/aspHI **DSIHKAI** bmyI psp1406I maell asp700 I CWX mbol I mbol/ndell[dam-] dpnII[dam-] alwI[dam-] dpnI[dam+] alwi[dam-] acii bstYI/xhoII sau3AI mbol/ndell[dam-] sau3AI nspBII berl dpnII[dam-] dpnI[dam+] bstYI/xhoII maelll taql

hpall BCLFI ncil dsav Idsm fnuDII/mvnI acil bstUI

scal hphi maelli 6301 GCTATGTGGC GCGGTATTAT CCCGTGATGA CGCCGGGCAA GAGCAACTCG GTCGCCGCAT ACACTATTCT CAGAATGACT TGGTTGAGTA CTCACCAGTC CGATACACCG CGCCATAATA GGGCACTACT GCGGCCCGTT CTCGTTGAGC CAGCGGCGGTA TGTGATAAGA GTCTTACTGA ACCAACTCAT GAGTGGTCAG ddeI begI beiEI bsoFI ahall/bsallI hgal caull hhal/cfol hinpi

fnu4HI

mcrI

hinll/acyl

**bsh1236I** 

mbol/ndell[dam-] dpnII[dam-] dpnI(dam+) pvuI/bspCI beiEI MCrI haeIII/palI fnu4HI cfrI eael **b**BoFI acii bbvI mslI nlaIII fnu4HI bsoFI

Bau3AI

cep61 bsrl

6401 ACAGAAAAGC ATCTTACGGA TGGCATGACA GTAAGAGAAT TATGCAGTGC TGCCATAACC ATGAGTGATA ACACTGCGGC CAACTTACTT CTGACAACGA TGTCITITCG IAGAAIGCCI ACCGIACIGI CATICICIIA AIACGICACG ACGGIATIGG TACICACIAI IGIGACGCCG GIIGAAIGAA GACIGIIGCI foki nlaiii BfaNI

mbol/ndell[dam-] alul hpall dpnII[dam-] bsaWI nlaiv dpnI[dam+] sau3AI mbol/ndell[dam-] Sau3AI maeIII dpnII(dam-) dpnI[dam+] nlaIII Bau96I avalI asuI

6501 TCGGAGGACC GAAGGAGCTA ACCGCTTTTT TGCACAACAT GGGGGATCAT GTAACTCGCC TTGATCGTTG GGAACCGGAG CTGAATGAAG CCATACCAAA AGCCTCCTGG CTTCCTCGAT TGGCGAAAAA ACGTGTTGTA CCCCCTAGTA CATTGAGCGG AACTAGCAAC CCTTGGCCTC GACTTACTTC GGTATGGTTT acil aluI mnlI

nlalli alwi[dam-]

			tru91	mseI	asel/asnl/vspl	ACANTTANTA	TGTTAATTAT
	hpall	I scrFI	ncil	dsav	Caull	CTTCCCGGCA	GAAGGGCCGT
		Inla	rmal	maeI	bfal	STTACTCTAG	SAATGAGATC
			berl	tru91	mseI	NTTANC TGGCGAACTA (	TAATTG ACCGCTTGAT
1,1011	hhal/cfol	mstI	avill/fspl	maeII	psp14061	A ACGITGCGCA AACI	T TGCAACGCGT TTGA
		fnu4HI	bsoFI	Cacal barni	faxi bbvi	. AATGGCAAC	GCTGCTCCCA CTGTGGTGT ACGGTCGTCG TTACCGTTGT TGCAACGCGT TTGATAATTG ACCGCTTGAT GAATGAGATC GAAGGCCCGT TGTTAATTAT
				1104	I Add INA A TITLE AND INC.	CONTRACTOR ECONOMICS	GCTGCTCGCA CTGTGGTGC

**bsmAI** beal 6701 GACTGGATGG AGGCGGATAA AGTTGCAGGA CCACTTCTGC GCTCGCCCCT TCCGGCTGGC TGGTTTATTG CTGATAAATC TGGAGCCGGT GAGCGTGGGT CIGACCIACE ICCGCCTAIT ICAACGICCI GGIGAAGACG CGAGCCGGGA AGGCCGACCG ACCAAAIAAC GACIAITIAG ACCICGGCCA CICGCACCCA cfr101/bsrFI bpmI/gsuI{dcm-} nlalv hphI hpall cacel hpall Idsm haeIII/palI .. sau96I hinpi asui hhaI/cfoI Bau96I avall asuI acil mnlI fokI bsrl

bgll

Idam

6801 CTCGCGGTAT CATTGCAGCA CTGGGGCCAG ATGGTAAGCC CTCCCGTATC GTAGTTATCT ACACGACGGG GAGTCAGGCA ACTATGGATG AACGAAATAG GAGCGCGCATA GTAACGTCGT GACCCCGGT TACCATTCGG GAGCGCCATA GTAACGTCGT GATACCTAC TTGCTTTATC fokI ahdi/eam11051 hinfI mn]I haeIII/palI 196nes nlaiv berl asul fnu4HI bsoFI bbvI bsh1236I berDI funDII/mvnI betul acil thal

tru91 6901 ACAGATCGCT GAGATAGGTG CCTCACTGAT TAAGCATTGG TAACTGTCAG ACCAAGTTTA CTCATATATA CTTTAGATTG ATTTAAAACT TCATTTTAA TGTCTAGGGA CTCTATCCAC GGAGTGACTA ATTCGTAACC ATTGACAGTC TGGTTCAAAT GAGTATATAT GAAATCTAAC TAAATTTTGA AGTAAAATT mBeI ahalll/dral tru9I meeI maelll tru9I mseI dpnI(dam+) hglCI
dpnII(dam-) banI mnlI nlaIV mpol/ndell[dam-] Bau3AI

ddeI

mbol/ndell[dam-] dpnII[dam-] dpnI[dam+] Bau3AI 7001 ITTAAAAGGA TCTAGGIGAA GAICCITIII GAIAAICICA IGACCAAAAT CCCITAACGI GAGIITICGI ICCACIGAGC GICAGACCCC GIAGAAAAGA малтттест абатеслет стаббалам статабает астбеттта беблатеса стелалабел абстбастее састетебе сатетттет  ${\rm FIG.}\,48V$ hgal ddeI maell tru9I meel nlaIII bspHI rcal mbol/ndell[dam-] dpnII[dam-] dpnI[dam+] alwi[dam-] bstYI/xhoII ahaili/drai bfai mboli[dam-] Bau3AI mpol/ndeII [dam-] sau3AI hphI dpnII[dam-] tru9I betYI/xhoII dpnI[dam+] alwI[dam-] rmal maeI mseI

	Sausai	mpol/ndell[dam-]	dpnI[dam+]	dpnII dam-	alwI[dam-]		hpall alul	GTTTGTTTGC CGGATCAGA	CANACANACG GCCTAGITICT
						acti	nspBII	ACCAGCGGTG	TGGTC3CCAC
							acli	NACCACCGCT	TTGGTGGCGA
								CANACANANA	GTTTGTTTT
			I u.	cacel	fnu4HI	bsoFI	ppvI	CTCCTCCTTC	GACGACGAAC
		1 thai		bstUI	<b>bsh1236</b> I	hinPI	hhal/cfof bbvl	TGCGCGTAAT	ACGCCCATTA
6au3AI	mbolI(dam-1	- mpol / ndell [dam - ]	]	dpnI[dam+] dpnI[dam+]	dpnII[dam-] dpnII[dam-]	betYI/xhoII alwI[dam-]	alwi[dam-] batYI/xhoII	7101 TCANAGGATC TICTIGAGAT CCTITITIC TGCGCGTAAT CTGCTGCTTG CAAACAAAAA AACCACCGCT ACCAGGGGGTG GTITGTITGC CGGATCAAGA	AGTITECTAG AAGAACTETA GGAAAAAAAG ACGCGCATTA GACGACGAAC GTITGTITIT TIGGIGGCGA IGGICSCCAC CAAACAAACG GCCIAGIICI

	haeIII/palI	TAGGCCACCA CTTCAAGAAC	CGATGGTTGA GAAAAAGGCT TCCATTGACC GAAGTCGTCT CGCGTCTATG GTTTATGACA GGAAGATCAC ATCGGCAICA ATCCGGIGGI GAAGILLIIG	
		bsli TAGCCGTAGT	ATCGGCATCA	
Thur	macI	bfal CCTTCTAGTG	GCAAGATCAC	
		CAAATACTGT	GTTTATGACA	InutHI
	hinPI	hhal/cfol GCGCAGATAC	CGCGTCTATG	
		eco57I CTTCAGCAGA	GAAGTCGTCT	
	bsrI	maelli AGGTAACTGG	TCCATTGACC	
		7201 GCTACCAACT CTTTTCCGA AGGTAACTGG CTTCAGCAGA GCGCAGATAC CAAATACTGT CCTTCTAGTG TAGCCGTAGT TAGGCCACCA CTTCAAGAAC	CGATGGTTGA GAAAAAGGCT	

rmal macI

				pleI	hinfi	TEGAC TCAAGACGAT
SCIFI	ncil	Idsm	hpall	dsav	Caull	GTCTTAC CGGGT
bsoFI	bbvI	fnu4HI	olen!	bsrI bsoFI	maelli bbvi bsri	SCTACATA
					T Just T and T	1 TCTGTAG AGACATO

dde	aluI	slw441/snol	hhal/cfol	macIII
•		apaLI/snoI	hinpi baiei	brawi
		bmyI	bbvI mcrI	hpall
		bsinkai	bsoFI	Idem
		bsp1286	fnu4HI	
		hgiAI/aspHI	nspBII	
			acii	

7401 AGTTACCGGA TAAGGCGCAG CGGTCGGGCT GAACGGGGG TTCGTGCACA CAGCCCAGCT TGGAGCGAAC GACCTACACC GAACTGAGAT ACCTACAGG TCAATGGCCT ATTCCGCGTC GCCAGCCCGA CTTGCCCCCC AAGCACGTGT GTCGGGTCGA ACCTCGCTTG CTGGATGTGG CTTGACTCTA TGGATGTCG

### FIG. 48W

ecoRII	daav	betni	beaJI	hhal/cfol alul apyl[dcm+]	GAGCTTCCA
		DBBSI	hinpi mnli	hhal/cfol	ACCCCACGAG G
					GGAACAGGAG
		hpall fnu4HI	bsoFI	acti	DESCRIPTION SALES
	Idsm	hpall	ball baoFI	beawi acti	ATCCGGTA
				acil	上がりないないがい かななないないかな
		10 5 74	bber /ofor	had! Ctot	ASSETTAGE GGARAGES ACCEDENCE ATCREATANCE AGGETTANG COCCARGOTT GGARACAGGAG ACCCARGAG GGAGCTTCCA

SCLFI INVE 7501 TGAGCATTGA GAAAGCGCCA CGCTTCCCGA AGGGAGAAAG GCGGACAGGT ATCCGGTAAGGGTC GGAAGAGAA AGCGTGCTG GCAGGAAGGGT ACTCGTAACT CTTTCGCGGT GCGAAGGGCT TCCCTCTTTC CGCCTGTCCA TAGGCCATTC GCCGTCCCAG CCTTGTCCTC TCGCGTGCTC CCTCGAAGGT

nlaIV taqi ecoRII scrFI betNI dsav MVAI

7601 GGGGGAAACG CCIGGIAICI TIAIAGICCI GICGGGIIIC GCCACCICIG ACTIGAGCGI CGAITITIGI GAIGCICGIC AGGGGGCCGC AGCCIAIGGA CCCCCTTIGC GGACCATAGA AATATCAGGA CAGCCCAAAG CGGTGGAGAC TGAACTCGCA GCTAAAAACA CTACGAGCAG TCCCCCGCC TCGGATACCT apyI[dcm+]

acti

efaNI

hqaI

mnll drdI

hinfi aflili nspHI haeIII/pall nspl nlalli haeI cacel haeIII/pall apyI[dcm+] mval bsll ecoRII nlaIV haeI bstNI BCLFI dsav haeIII/palI fnuDII/mvnI thal ball **bsh1236I** fnu4HI **baoFI** acil betuI

7701 AAAACGCCAG CAACGCGCCC TITITACGGT TCCTGGCCTT TTGCTCACA TGTTCTTTCC TGCGTTATCC CCTGATTCTG TGGATAACCG TTTGCGGTC GITGCGCCGG AAAAATGCCA AGGACCGGAA AACGACCGGA AAACGAGTGT ACAAGAAAGG ACGCAATAGG GGACTAAGAC ACCTATTGGC cacel

mboli hhal/cfol earI/ksp632I sapI hinPI acti mnlI hinpi hinfi bbvI pleI hhaI/cfoI fnu4HI **b**BoFI bsiEI fnu4HI bsoFI bbvI **barBI** fnu4HI cac81 ac11 bsoFI acil aluI

7801 TATTACCGCC TTTGAGTGAG CTGATACCGC TCGCCGCAGC CGAACGACCG AGCGCAGCGA GTCAGTGAGC GAGGAAGCGG AAGAGCGCCC AATACGCAAA ATAATGGGGG AAACTCACTC GACTATGGCG AGGGGGGTCG GCTTGCTGGC TCGCGTCGCT CAGTCACTCG CTCCTTCGCC TTCTCGCGGG TTATGCGTTT

haeII

FIG. 48X

maeIII hhal/cfol asel/asnl/vspl 7901 CCGCCTCTCC CCGCGCGTTG GCCGATTCAT TAATCCACT GCCACGACAG GTTTCCCGAC TGGAAAGCGG GCAGTGAGCG CAACGCAATT AATGTGAGTT GCCTCAA GCCGGAGAGG GCGCGCAAC CGGCTAAGTA ATTAGGTCGA CCGTGCTCAA ACCTTTCGCC CGTCACTCGC GTTGCGTTAA TTACACTCAA tru9I mseI hinPI berBI cacel acil bsrIhpaII mspI eael tfil asel/asnl/vspl cfrI hinfI mseI nspBII tru9I pvuII hgici apyi [dcm+] ecoRII scrFI nlaIV bstNI dsav banl baaJI IDVE bsh1236I ball acii mnll acii

cacel

aluI

haeIII/pall

bstul

fuuDII/mvnI

hhal/cfol

thal

hinpi

Invm/IIdun1

thaI

**bsh1236**I

betui

FIG. 48Y

8001 ACCTCACTCA TTAGGCACCC CAGGCTTAC ACTTTATGCT TCGGGCTGGT ATGTTGTGTG GAATTGTGAG GGGATAACAA TTTCACACAG GAAACAGCTA TGGAGTGAGT AATCCGTGGG GTCCGAAATG TGAAATACGA AGGCGAGGA TACAACACAC CTTAACACTC GCCTATTGTT AAAGTGTGTC CTTTGTCGAT

```
3562 3566 3676 3733 3792 4270 4288 4311 4344 4554 4842 4896 4954 5047 5333 5590
5803 5822 6516 6579 6679 7200 7457 7593 7819 7937 8096
                                                                                                                                                                                 3167 3179 3188 3200 3210 3221 3267 3372 3404 3449 3686 3949 4021 4318 4542 4727 4739 4748 4760 4770 4781 4827 4910 4914 5070 5127 5153 5166 5203 5217 5220 5248 5275 5680 5699 5741 5751 5790 5979 6026 6125 6234 6311 6355 6476 6522 6713 6804 7166 7175 7310 7420 7541 7560 7687 7715 7806 7827 7834 7877 7901 7911 7967 8070
                                                                                                                                                     217 229 238 250 260 271 317 422 454 485 574 1385 1795 1871 2248 2250 2758 2982
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   5 44 332 386 390 753 1097 1165 1370 1431 1951 2603 2751 2784 3282 3336 3340
                                                                                                                                                                                                                                                                                                                                                                                                                                                             988 1690 1858 5117 5947 6329
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          696 4935 6290 6982 7001
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         1876 5651 6198 7444
                                                                                                                             823 1039 2738 4237
                                                                                            2969 3967 4529
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           ahdi/eam11051(GACNNNNGTC): 2087 6865
                                                                1690 5947
                                                                                                                                                                                                                                                                                                                                  see hinll
                                                                                                                                                                                                                                                                                                                                                                                                932 7758
                                                                                                                                                                                                                                                                                                                                                                                                                                 1833
                                                                                                                                                                                                                                                                                                                                                               982
                                                                                                                                                                                                                                                                                                                                                                                                                                                             ahali/beahi (GRCGYC):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               ahalii/drai(TTTAAA):
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                alw44I/snoI(GTGCAC):
                                                                                                                                                                                                                                                                                                                                                                   aflii/bfri(CTTAAG):
                                                                                                                                                                                                                                                                                                                                                                                                  aflili(ACRYGT):
                                                                                                   acc651 (GGTACC):
                                                                  aatii(GACGTC):
                                                                                                                                  accI (GTMKAC):
                                                                                                                                                                                                                                                                                                                                                                                                                                      age I (ACCGGT):
>length: 8120
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               aluI (AGCT):
                                                                                                                                                                      acil(CCCC):
```

BIOI TGACCATGAT TACGATTAA (SEQ ID NO:68) ACTGGTACTA ATGCTTAATT

asp700 Iumx

nlalII

asel/asnl/vspl

tru91

mseI

FIG. 48Z

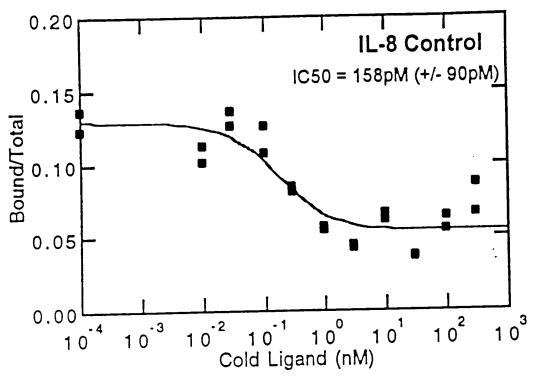


FIG. 49A

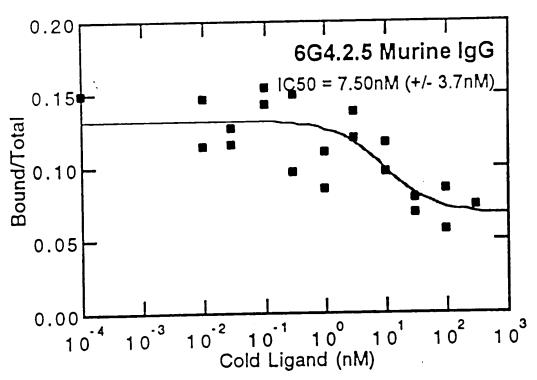


FIG. 49B

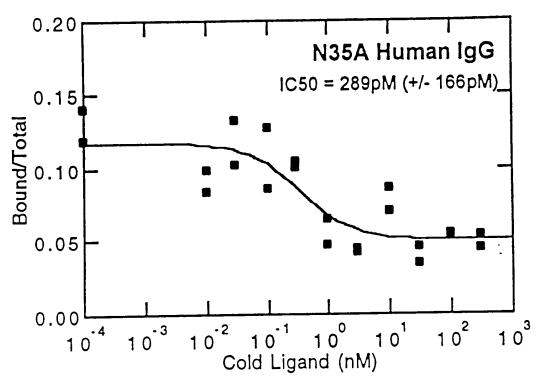


FIG. 49C

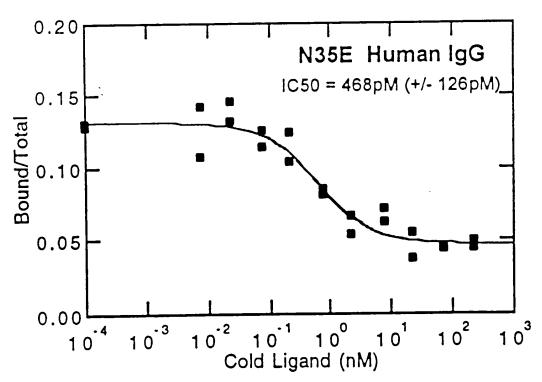


FIG. 49D

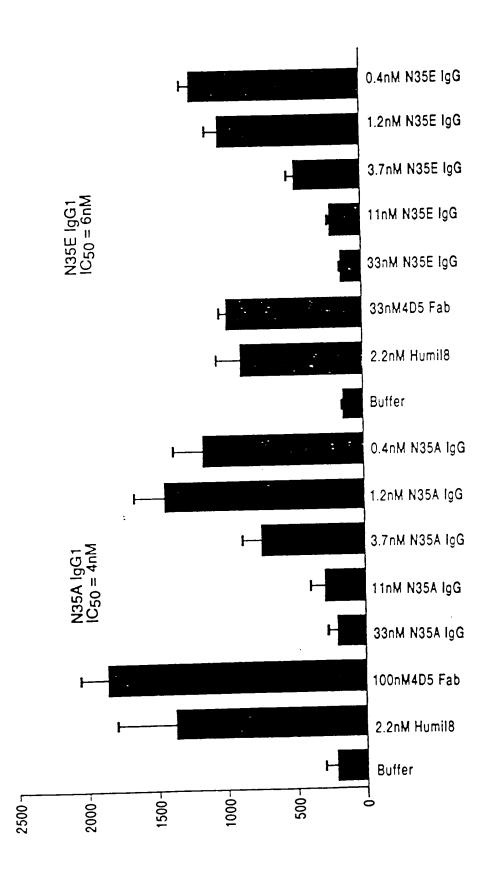
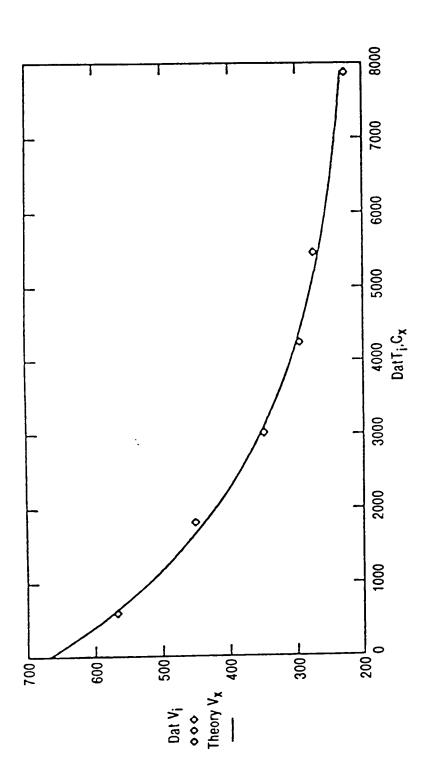


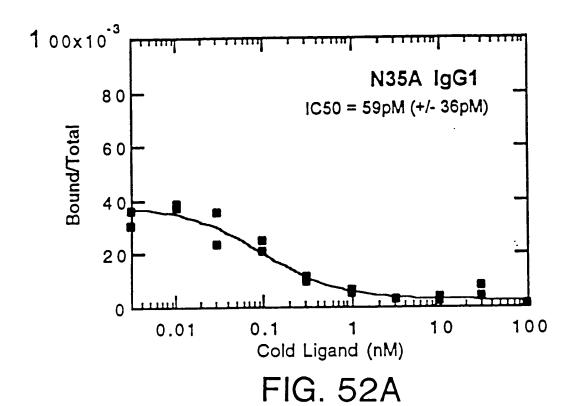
FIG. 50A

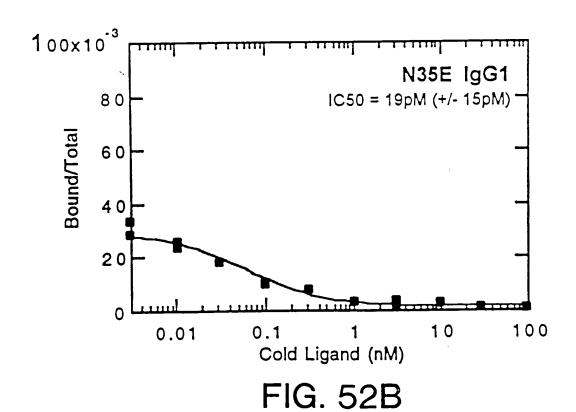
FIG. 50B



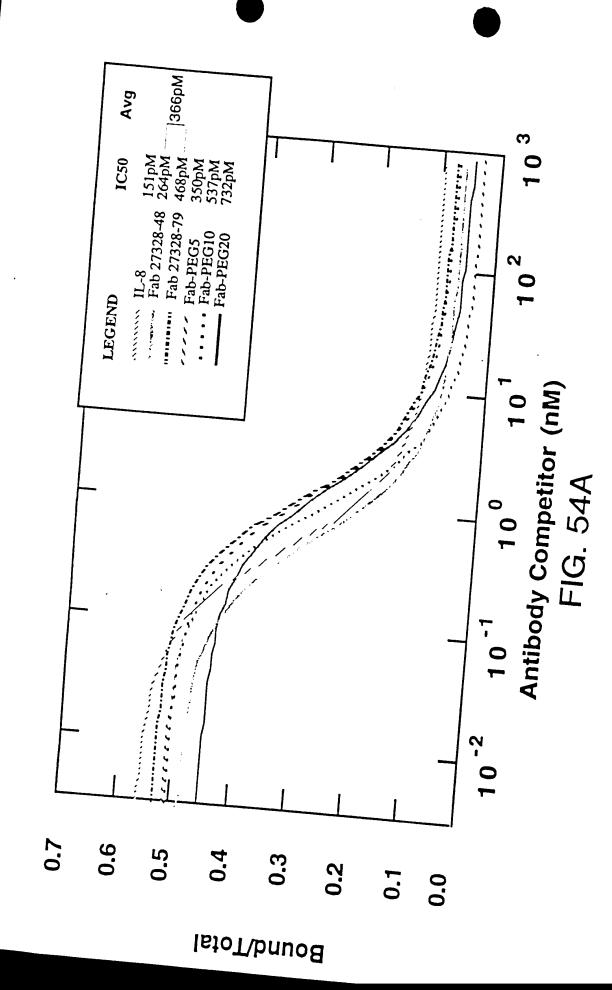
Representative Conc versus Time Plot. Shown is the kinetic data for 6G4V11N35A.IgG1

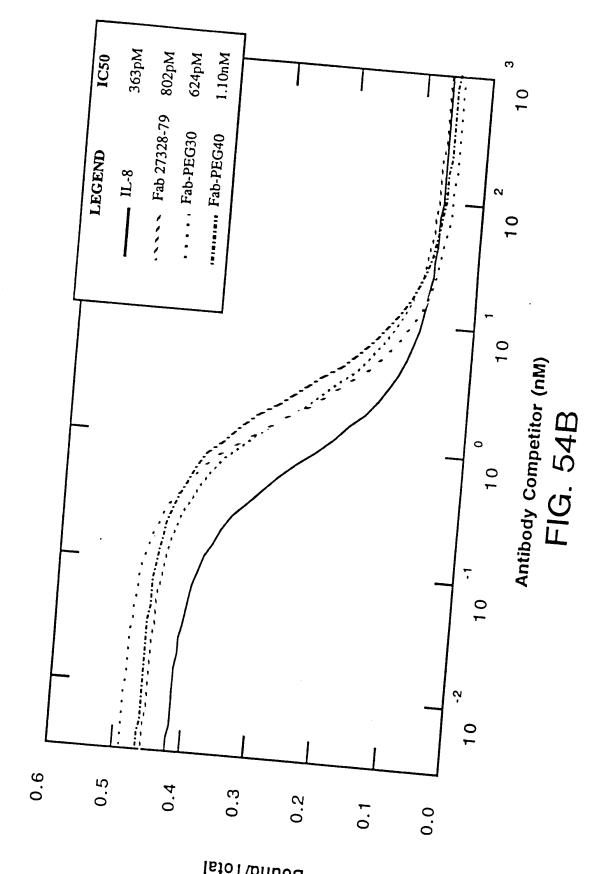
[		FIG. 51							
Kd	350pM	88pM	49pM						
kd	2.9x10 <sup>-4</sup>	$7.7x10^{-5}$	$1.4 \times 10^{-4}$						
ka	8.3x105	$8.7x10^{5}$	$3.0 \times 10^{6}$						
SAMPLE	Murine 6G4.2.5 IgG2a	6G4V11N35A-IgG1	  6G4V11N35E-IgG1						



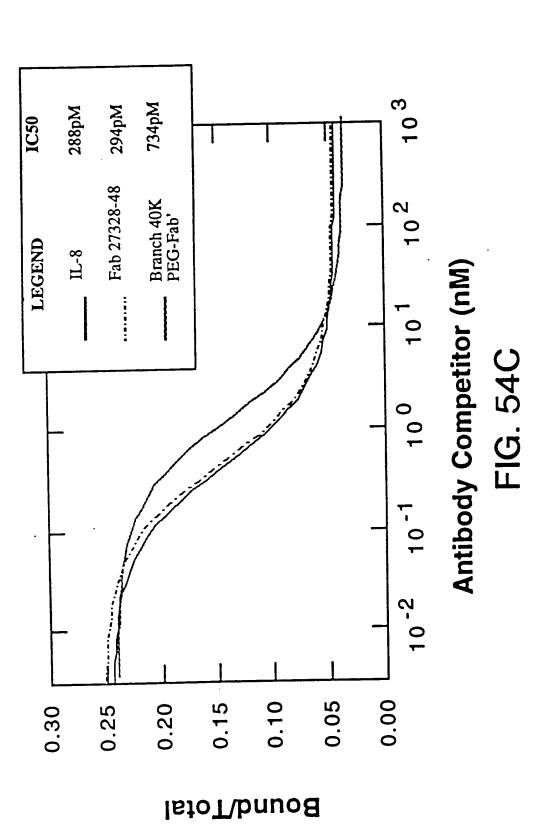


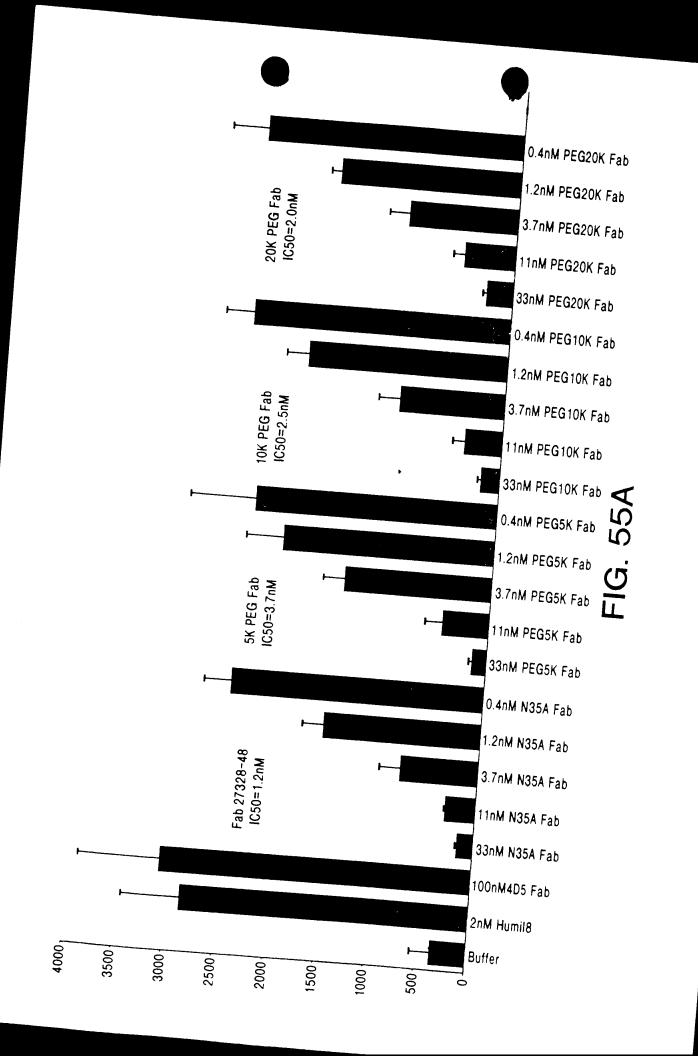
781	AAAAGGG	TAT	CTAGA	AGGTTY ICCAA	AGC	TGA'	AAAA	TAG	CL-L-	LLLCI	TAT	AGCG	TAA	AGA	AGAA	ACGT.
-1								M	K	K 1	1 1	А	r	L	L	A
	TCTATGT AGATACI	A ACC	ממממ	ነ አር አጥ	A ACC	CYTAS	TTTG	CG	CATO	GCGAC	: TCC	AAGT	CGA	TCA	cor	LAGA
-11	S M I	V	F	s I	A	Т	N	A	Y	A F	e v	Q	L	V	Q	S
901	GGCGGT	GCC	TGGT	GCAGC	AGO	GGG	CTCA	CTY	CCG	TTGT	CCT	GTGC	AGC	TTC:	TGG(	CTAC
8		CCGG	V	Q P	G	G	S	L	R	LS	C C	A	A	S	<u>G</u>	Y
961	TCCTTC	rcga	GTCAG	CTATA	r gcz	ACTG	GGTC	ÇG'	TCA	GCC	CGG	GTAA	GGG	CCTY	GGA	ATGG
	AGGAAGZ	CCT	CACTY	TATAS	A CG1	<b>IGAC</b>	CCAG	GC.	AGTY		GCC	CATI	CCC	GGA	CCT.	TACC
	GTTGGA'															
	CAACCT	ጥልጥል	እ እ ርጥን	ACCAA	GT	PACC	ACTT	TG.	ATG(	CATA	r TAG	LaLaLaI	CAA	GIT	CCC	SGCA.
48	V G	<u> </u>	D	P S	N	<u> </u>	_E	T	<u>T</u> _	<u>Y_1</u>	4 C	K_	_F_	K	<u> </u>	R
1081	TTCACT	TAT	CTCG	CGACA	A CTY	CAA	AAAC	AC.	AGC.	ATAC	TGC	AGAT	AAD TTO	CAG	CCTY	GCGT CGCA
68	AAGTGA	AATA L S	GAGC(	D N	r GAC S	K	N	T	A	Y		M	N	s	L	R
1141	GCTGAG	GACA	CTGC	CGTCT	A TT	ACTG	TGCA	ΑG	AGG	GGAT	OTA 1	GCTA	CAA	TGG	TGA	CTGG
	CGACTC	ጥርም	GACGO	GCAGA <sup>1</sup>	r aar	<b>IGAC</b>	ACGT	TC	TCC	CCTA	A TAC	CGAT	GTT	ACC	ACT	GACC
1201	TTCTTC	GACG	TCTG	GGGTC	A AGG	SAAC TTTC	CCTG	GT CA	CAC GTG	CGTC' GCAG	r cci A gga	`CGG(	CTC	CAC GTG	CAA! GTT:	GGGC CCCG
108_	F F	D_Y	W	G Q	G	т	L	V	T	V :	s s	A	s	T	K	G
1261	CCATCG	STCT	TCCC	CCTGG	C AC	CCTC	CTCC	AA	GAG	CACC'	r cro	GGGG	CAC	AGC	GGC	CCTG
128	GGTAGC P S	CAGA V F	AGGG	GGACC L A	G TG( P	GGAG S	GAGG S	TT K	CTC S	GTGG: T :	A GAC	CCCC	:GTG T	A A	A.	GGAC L
	GGCTGC															
	CCGACG	CACC	YC44	CCTGA	T GA	AGGG	GCTT	GG	CCA	CTGC	C ACA	GCAC	CTT	GAG	TCC	والالوك
	G C															
1381	CTGACC	AGCG	GCGT	GCACA	CCT	TCCC	GGCT	GT	TOO'	ACAG'	r cci	CAGO GTCC	ACT TYGA	CTA	CTC	CCTC GGAG
168	GACTGG L T	rege S G	V	H T	F	P	A	V	L	Q	s s	G	L	Y	S	L
1441	AGCAGC	GTGG	TGAC	CGTGC	C CT	CCAG	CAGC	TI	GGG	CACC	C AGA	CCTA	ACAT	CTG	CAA	CGTG
	TCGTCG	CACC	ACTG	GCACG	G GA	GGTC	GTCG	AA	'CCC	GTGG	G TCI	GGAT	GTA	GAC	GTT	GCAC
	AATCAC	רדירכ	CCTC	GTTGT	G GT	TCCA	GCTG	Tal	CTT	TCAA	CTCC	GGT.	TAG	AAC	CACT	GTTT
208	N H	K P	S	r n	K	V	D	K	K	V	E I	K	s	С	D	K
1561	ACTCAC	ACAT	GCCC	GCCGI	GA C	SEQ:	IO NO:	69)	)							
228	TGAGTG T H	TGTA T C	. CGGG P	P C	.CT	Г	_1/	•	_	2						
	_		(SEQ	10 NO	00	t	-10	7.	J	3						

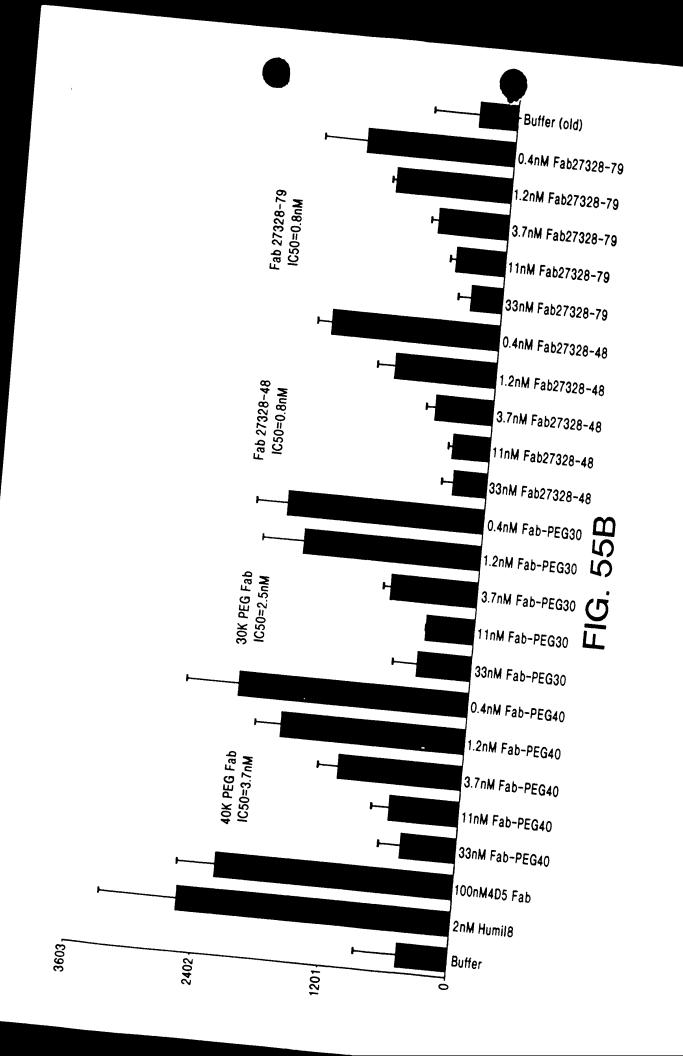


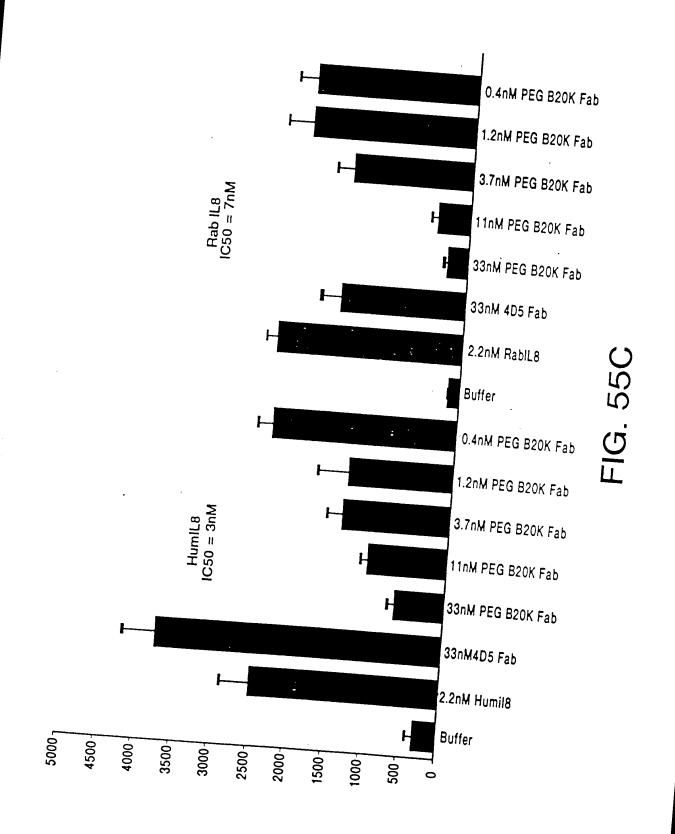


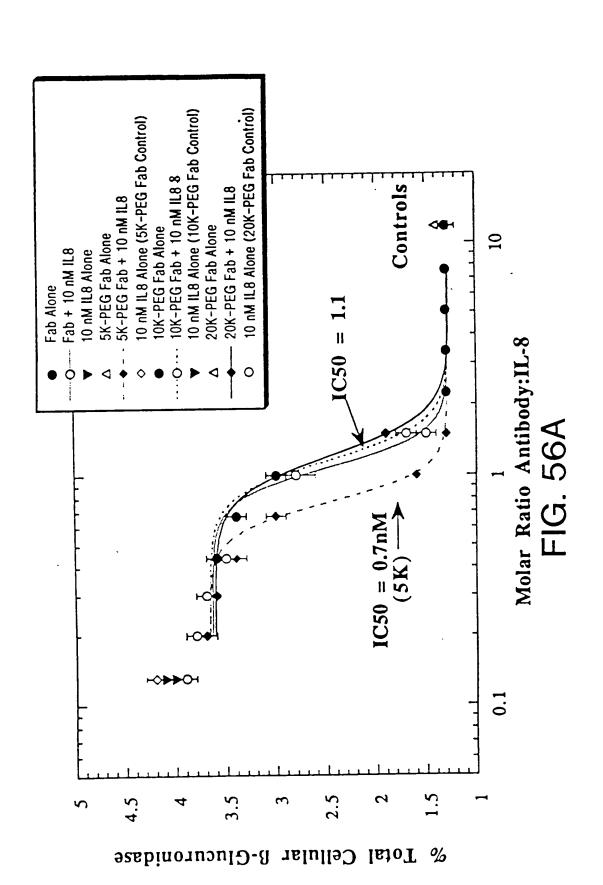
**Bound/Total** 

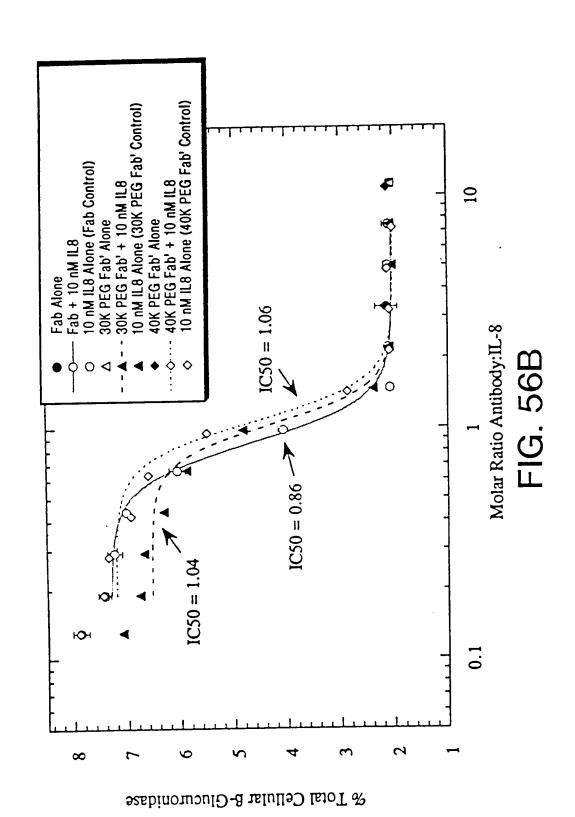




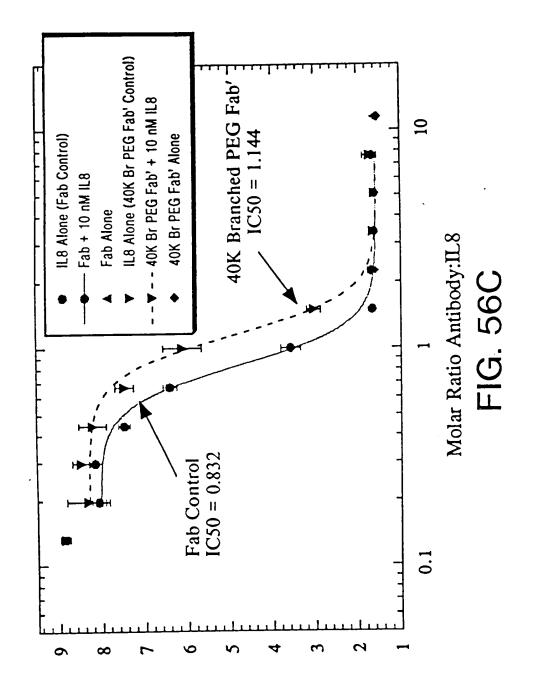


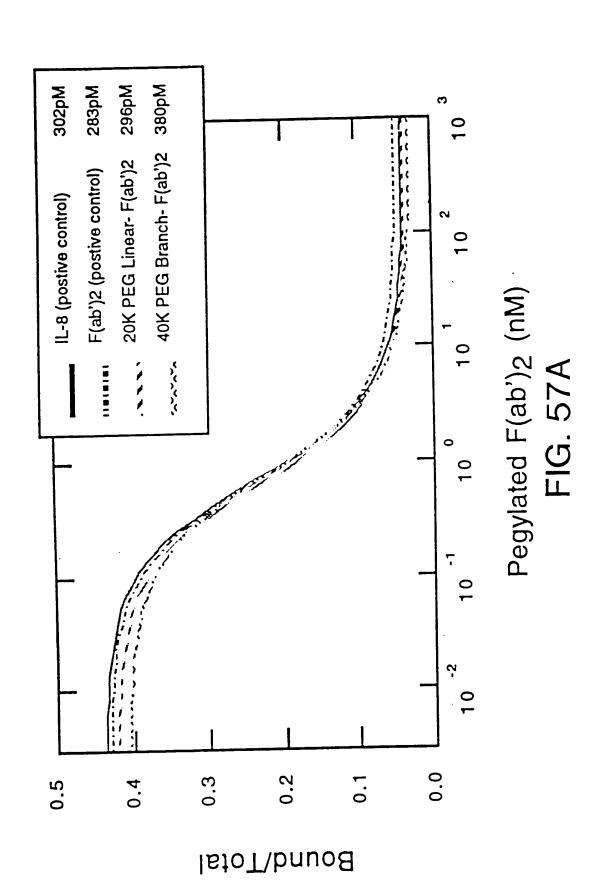


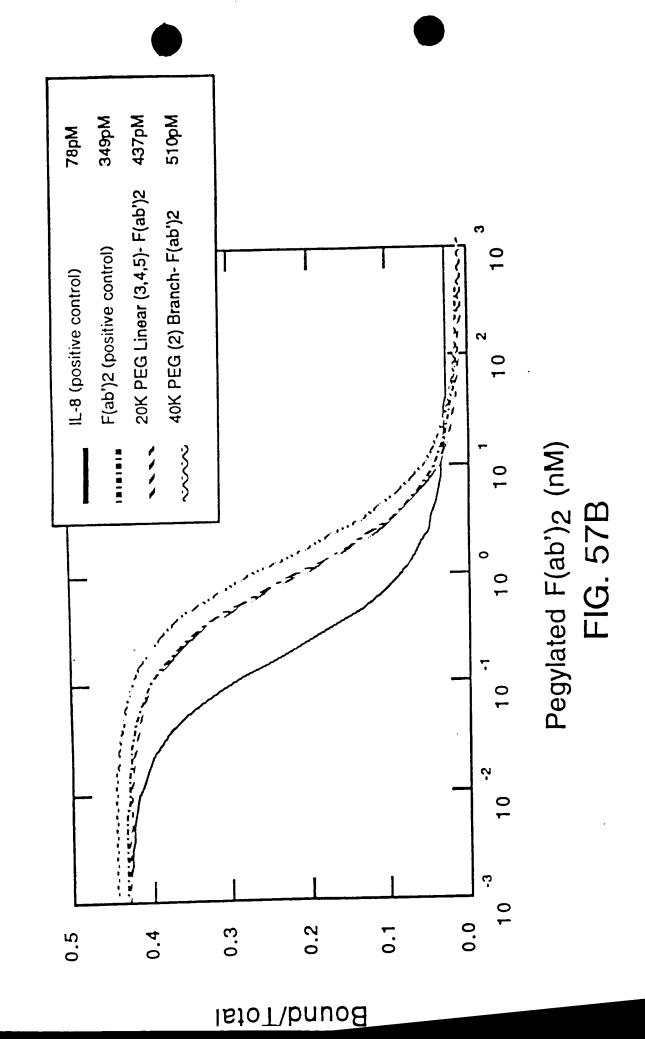


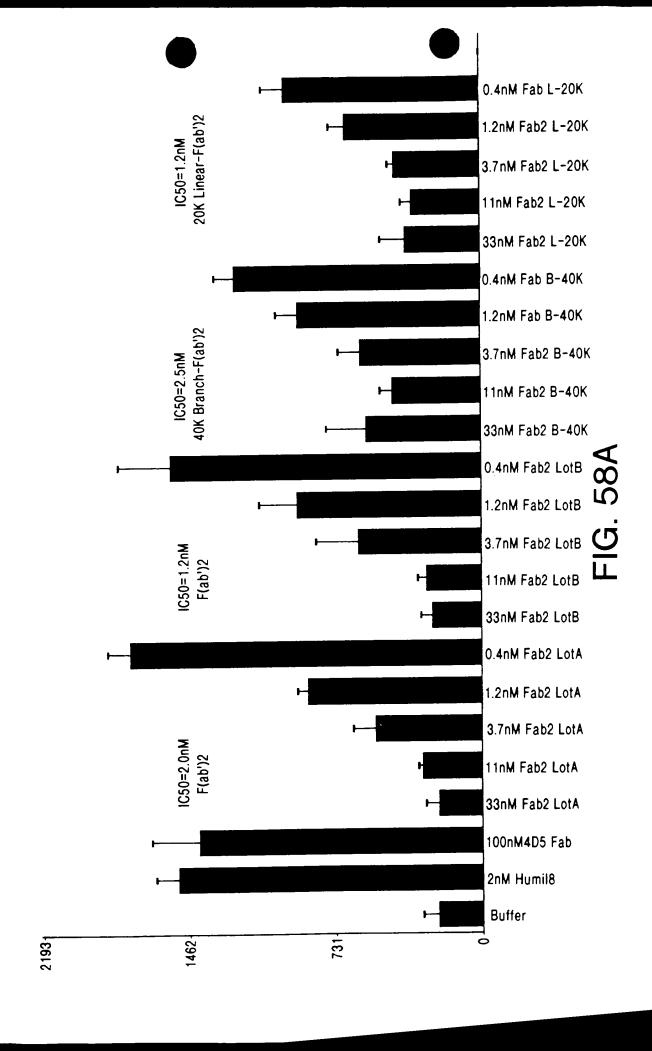


% Total Cellular B-Glucuronidase Activity









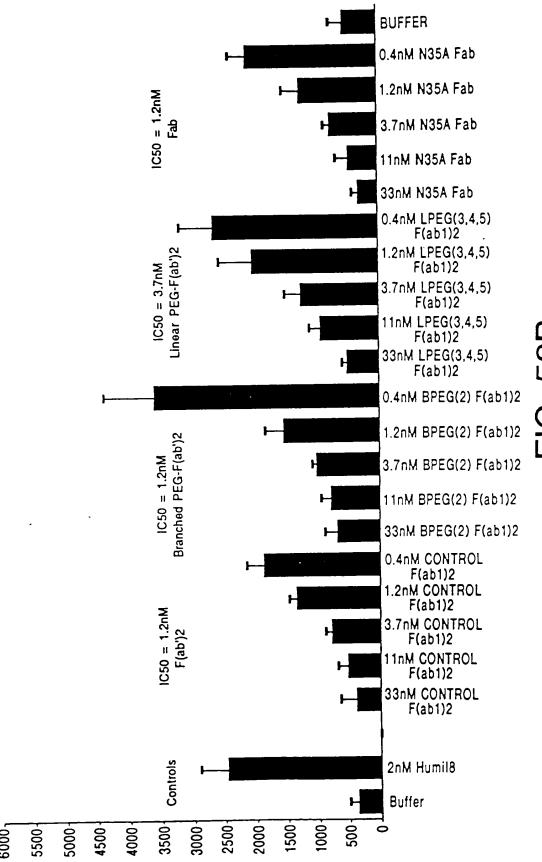
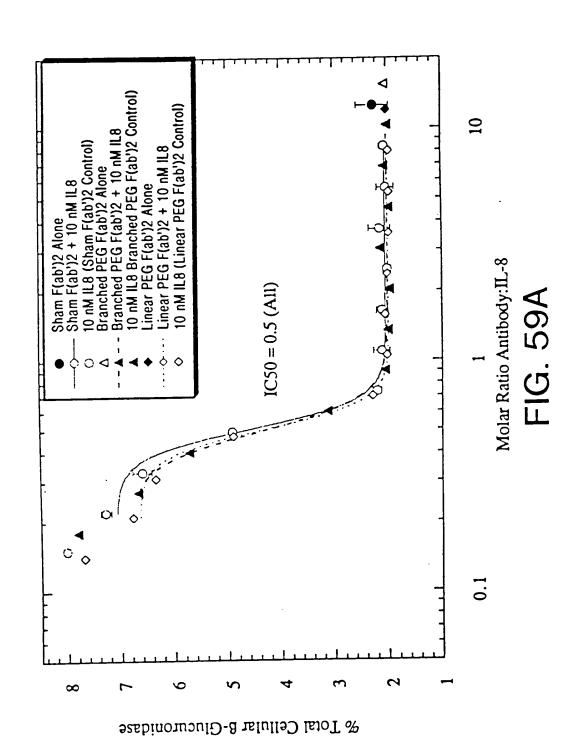
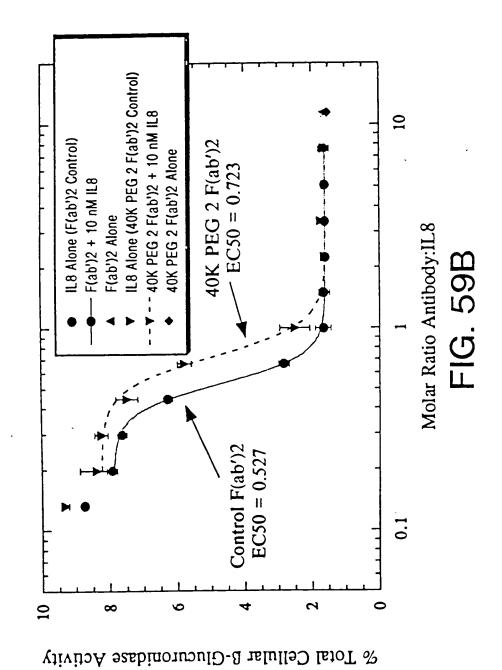
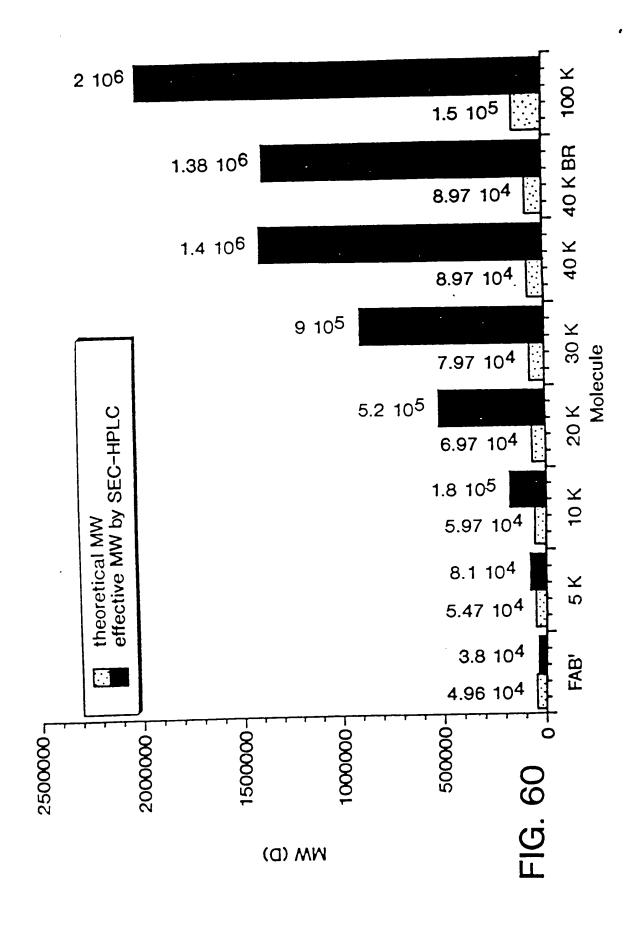
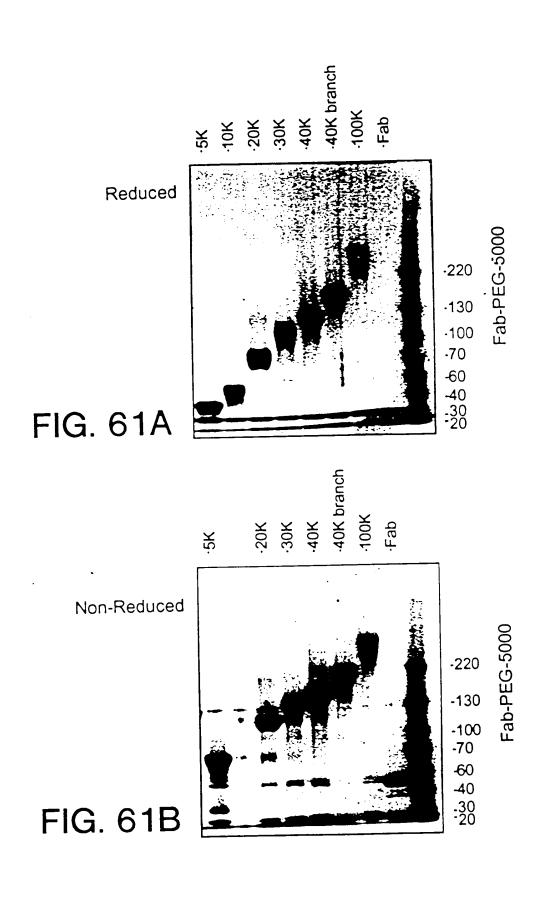


FIG. 58B









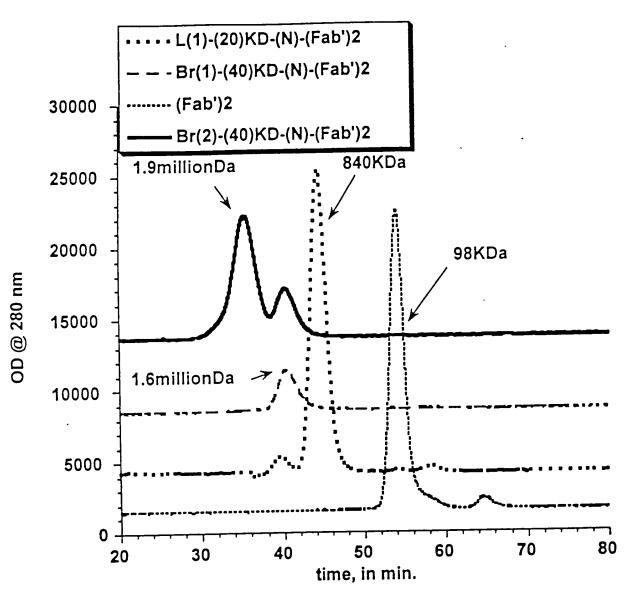


FIG. 62

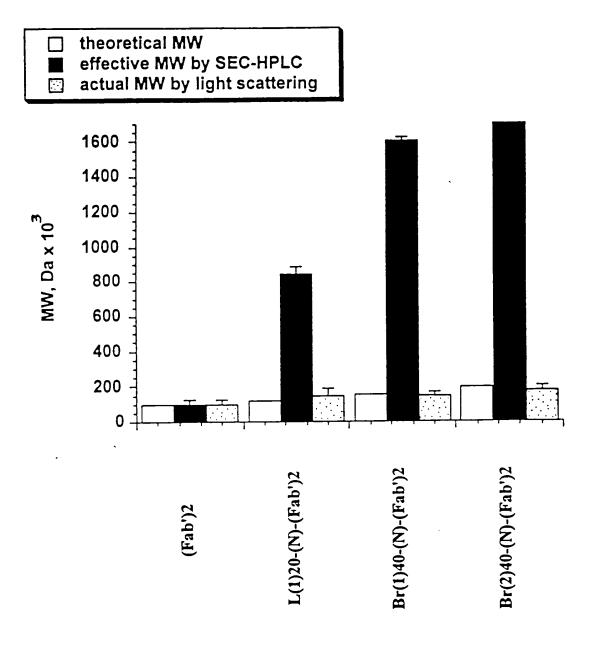


FIG. 63

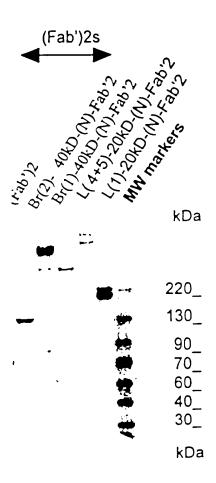
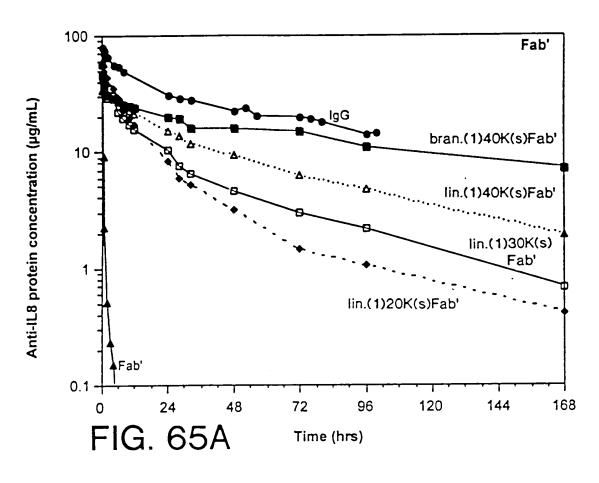
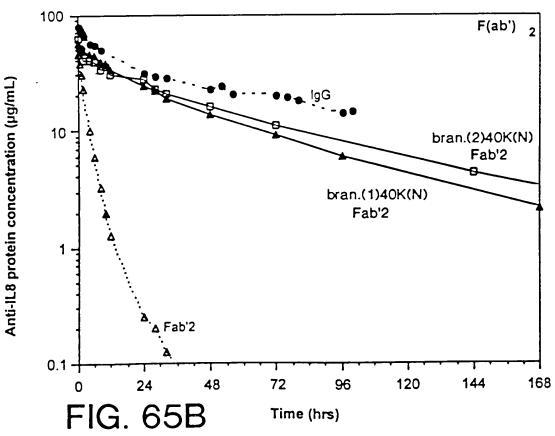


FIG. 64





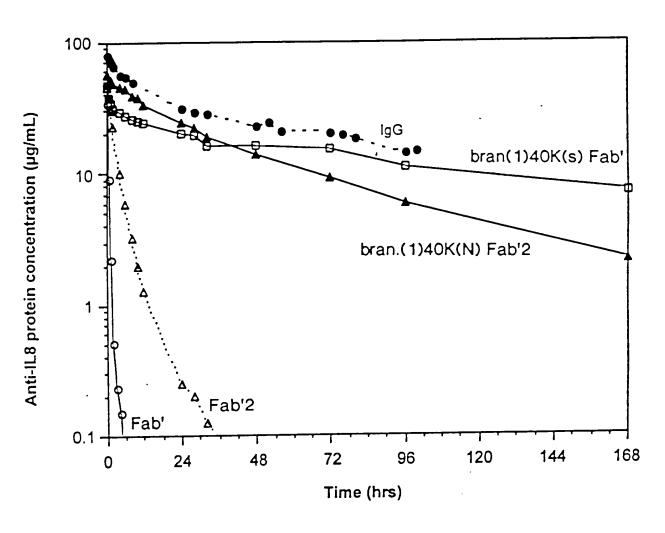
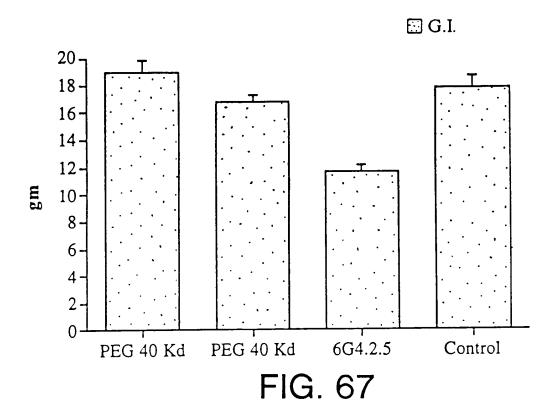
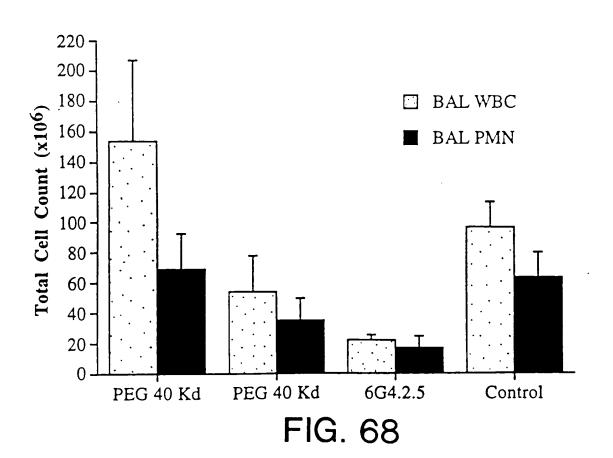


FIG. 66





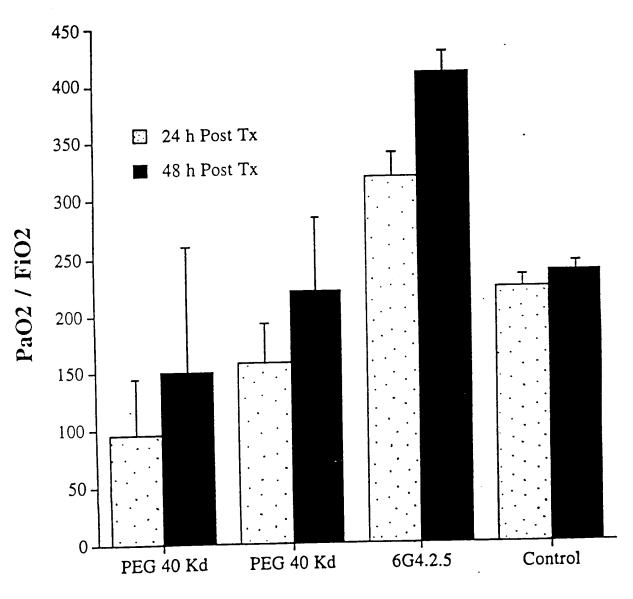
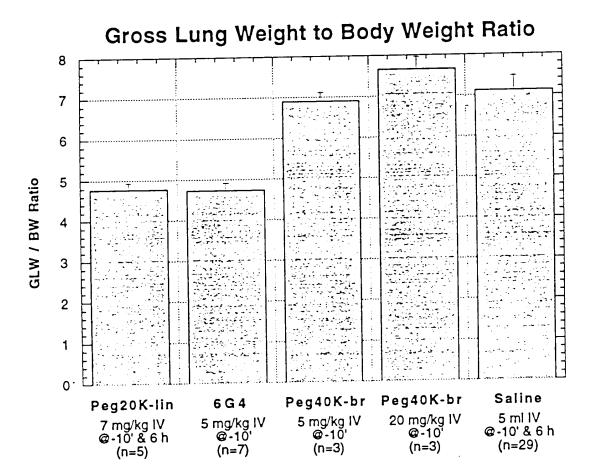
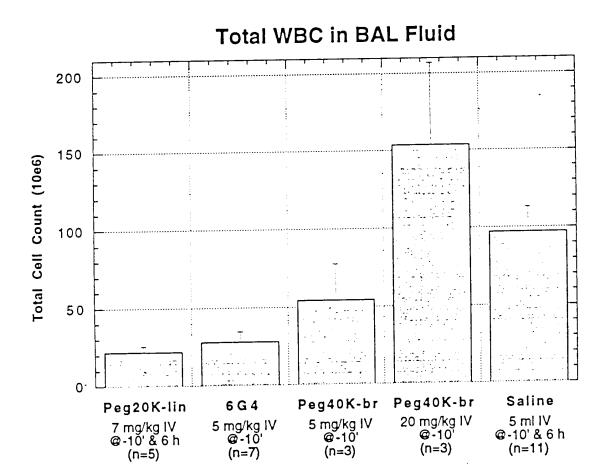


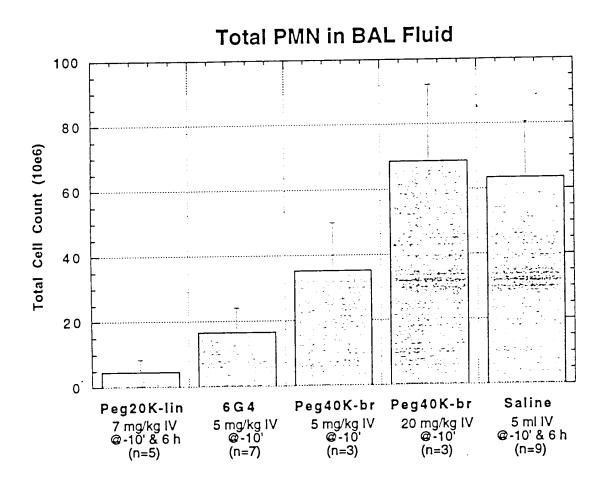
FIG. 69

## Oxygenation in 100% O2 @24 h Post Anti-IL8 Tx 500 400 PaO2 (mmHg) 300 200 100 0 Peg40K-br Peg40K-br Saline Peg20K-lin 6 G 4 5 ml IV @-10' & 6 h (n=25) 20 mg/kg IV @-10' (n=2) 7 mg/kg IV @-10' & 6 h (n=5) 5 mg/kg IV @-10' 5 mg/kg IV @-10' (n=3)(n=7)

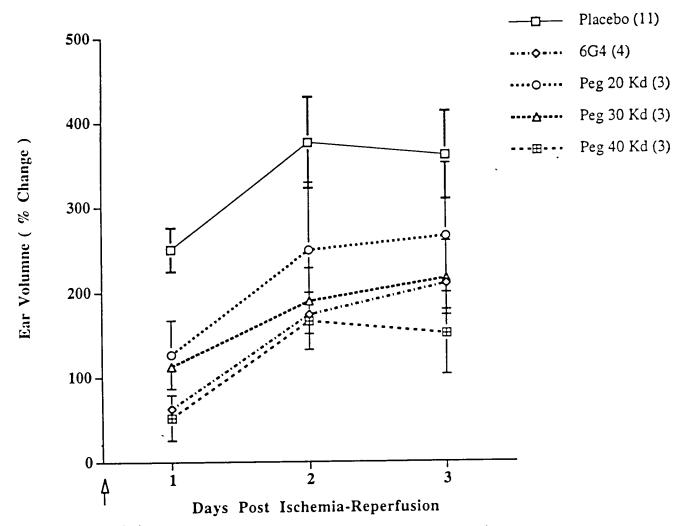
## Oxygenation in 100% O2 @48 h post Anti-IL8 Tx 500 400 PaO2 (mmHg) 300 200 100 0. Peg40K-br Saline Peg40K-br Peg20K-lin 6 G 4 20 mg/kg IV @-10' (n=2) 5 ml IV @-10' & 6 h (n=16) 5 mg/kg IV @-10' 5 mg/kg IV @-10' 7 mg/kg IV @-10' & 6 h (n=7)(n=3)(n=5)







## The Effect of Pegylated Anti-IL-8 in the Rabbit Ear model of Ischemia-Reperfusion Injury



Anti-IL-8 formulations: Single Dose (5 mg/kg) administered IV at time of reperfusion